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(54) Title: PROGNOSTIC CLASSIFICATION OF ENDOMETRIAL CANCER

(57) Abstract: The invention provided sets of genes that are expressed differentially in normal and malignant endometrium. These sets of genes can be used to discriminate between normal and malignant endometrial tissues. Accordingly, diagnostic assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens and monitoring tumor progression/regression also are provided.

PROGNOSTIC CLASSIFICATION OF ENDOMETRIAL CANCER

Field of the Invention

The invention relates to nucleic acid microarray markers for cancer, particularly for endometrial cancer. The invention also relates to methods for diagnosing cancer as well as optimizing cancer treatment strategies.

Background of the Invention

Endometrioid endometrial adenocarcinomas are the most common gynecologic malignancy, the risk of which is increased by an abnormal endocrine environment or premalignant lesions with loss of tumor suppressor function. The 6000 deaths yearly make uterine cancer the seventh leading cause of death from malignancy in females. It is primarily a disease of postmenopausal women, although 25 percent of cases occur in women below age 50 and 5 percent below age 40 (Harrison's Principles of Internal Medicine 1998).

Although much progress has been made toward understanding the biological basis of cancer and in its diagnosis and treatment, it is still one of the leading causes of death in the United States. Inherent difficulties in the diagnosis and treatment of cancer include among other things, the existence of many different subgroups of cancer and the concomitant variation in appropriate treatment strategies to maximize the likelihood of positive patient outcome.

The prognosis of endometrial cancer depends upon stage, histologic grade, and extent of myometrial invasion. The staging of endometrial cancer requires surgery to establish the extent of disease and the depth of myometrial invasion. Peritoneal fluid should be sampled; the abdomen and pelvis explored; and pelvic and para-aortic lymphadenectomy performed depending upon the histology, grade, and depth of invasion in the uterine specimen on frozen section.

Initial evaluation of patients suspected of endometrial cancer includes a history and physical and pelvic examination followed by an endometrial biopsy or a fractional dilation and curettage. Outpatient procedures such as endometrial biopsy or aspiration curettage can be used but are definitive only when positive. Once a diagnosis is made, the options for treating endometrial cancer are assessed with respect to the needs of the patient. These options traditionally include surgical intervention, radiotherapy, chemotherapy, and adjuvant systemic therapies. Adjuvants may include but are not limited to chemotherapy, radiotherapy, and

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endocrine therapies with progestational agents such as hydroxyprogesterone, megastrol, and deoxyprogesterone, and the antiestrogen tamoxifen.

It is difficult to predict from standard clinical and pathologic features the clinical course of endometrial cancer. However, it is very important in the treatment of endometrial cancer to select and implement an appropriate combination of therapeutic approaches. The available methods for designing strategies for treating endometrial cancer patients are complex and time consuming. The wide range of cancer subgroups and variations in disease progression limit the predictive ability of the healthcare professional. In addition, continuing development of novel treatment strategies and therapeutics will result in the addition of more variables to the already complex decision-making process involving matching the cancer patient with a treatment regimen that is appropriate and optimized for the cancer stage, extent of myometrial invasion, tumor growth rate, and other factors central to the individual patient's prognosis. Because of the critical importance of selecting appropriate treatment regimens for endometrial cancer patients, the development of guidelines for treatment selection is of key interest to those in the medical community and their patients. Thus, there presently is a need for objective, reproducible, and sensitive methods for predicting endometrial cancer patient outcome and selecting optimal treatment regimens.

Summary of the Invention

It now has been discovered that particular sets of genes are expressed differentially in normal and malignant endometrium. These sets of genes can be used to discriminate between normal and malignant endometrial tissues. Accordingly, diagnostic assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens, and monitoring tumor progression/regression can now be based on the expression of sets of genes.

According to one aspect of the invention, methods for diagnosing endometrial cancer in a subject suspected of having endometrial cancer are provided. The methods include obtaining from the subject an endometrial tissue sample and determining the expression of a set of nucleic acid molecules or expression products thereof in the endometrial tissue sample. The set of nucleic acid molecules includes at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50. In preferred embodiments, the endometrial tissue sample is suspected of being cancerous.

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In some embodiments the set of nucleic acid molecules includes more than 2, and up to all of the nucleic acid molecules set forth as SEQ ID NOs:1-50, and any number of nucleic acid sequences between these two numbers. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the nucleic acid molecules set forth as SEQ ID NOs:1-50.

In other embodiments, the method further includes determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the endometrial tissue sample suspected of being cancerous and the non-cancerous endometrial tissue sample.

The invention in another aspect provides solid-phase nucleic acid molecule arrays. The arrays have a cancer gene marker set that consists essentially of at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-50 fixed to a solid substrate. The set of nucleic acid markers can include any number of nucleic acid sequences between these two numbers, selected from SEQ ID NOs:1-50. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the nucleic acid molecules set forth as SEQ ID NOs:1-50. In some embodiments, the solid-phase nucleic acid molecule array also includes at least one control nucleic acid molecule.

In certain embodiments, the solid substrate includes a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. Preferably the substrate is glass.

In other embodiments, the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

According to yet another aspect of the invention, protein microarrays are provided. The protein microarrays include antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate. In some embodiments, the microarray comprises antibodies or antigen-binding fragments thereof, that bind specifically to least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 different polypeptides selected from the group consisting of SEQ ID NOs:51-100. In certain embodiments, the microarray also includes an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated

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polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100, preferably An endometrial cancer associated polypeptide. In some embodiments, the protein microarray also includes at least one control polypeptide molecule. In further embodiments, the antibodies are monoclonal or polyclonal antibodies. In other embodiments, the antibodies are chimeric, human, or humanized antibodies. In some embodiments, the antibodies are single chain antibodies. In still other embodiments, the antigen-binding fragments are F(ab')₂, Fab, Fd, or Fv fragments.

According to yet another aspect of the invention, protein microarrays are provided. The protein microarrays include antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate. In some embodiments, the microarray comprises antibodies or antigen-binding fragments thereof, that bind specifically to least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 different polypeptides selected from the group consisting of SEQ ID NOs:51-100. In certain embodiments, the microarray also includes an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100, preferably an endometrial cancer associated polypeptide. In some embodiments, the protein microarray also includes at least one control polypeptide molecule. In further embodiments, the antibodies are monoclonal or polyclonal antibodies. In other embodiments, the antibodies are chimeric, human, or humanized antibodies. In some embodiments, the antibodies are single chain antibodies. In still other embodiments, the antigen-binding fragments are F(ab')₂, Fab, Fd, or Fv fragments.

In a further aspect of the invention, methods for identifying lead compounds for a pharmacological agent useful in the treatment of endometrial cancer are provided. The methods include contacting an endometrial cancer cell or tissue with a candidate pharmacological agent, and determining the expression of a set of nucleic acid molecules in the endometrial cancer cell or tissue sample under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of expression of the set of nucleic acid molecules. The set of nucleic acid molecules includes at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-50. The methods also include detecting a test amount of the expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the presence of

the candidate pharmacological agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent that is useful in the treatment of endometrial cancer.

In some embodiments of any of the foregoing methods and products, the differences in the expression of the nucleic acid molecules are determined by nucleic acid hybridization or nucleic acid amplification methods. Preferably the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array. In other embodiments, the differences in the expression of the nucleic acid molecules are determined by protein expression analysis, preferably SELDI mass spectroscopy.

These and other aspects of the invention will be described in greater detail below.

Detailed Description of the Invention

The invention described herein relates to the identification of a set of genes expressed in endometrial cancer tissue that are predictive of the clinical outcome of the cancer. Changes in cell phenotype in cancer are often the result of one or more changes in the genome expression of the cell. Some genes are expressed in tumor cells, and not in normal cells. In addition, different genes are expressed in different subgroups of endometrial cancers, which have different prognoses and require different treatment regimens to optimize patient outcome. The differential expression of endometrial cancer genes can be examined by the assessment of nucleic acid or protein expression in the endometrial cancer tissue.

The genes identified permit, *inter alia*, rapid screening of cancer samples by nucleic acid microarray hybridization or protein expression technology to determine the expression of the specific genes and thereby to predict the outcome of the cancer. Such screening is beneficial, for example, in selecting the course of treatment to provide to the cancer patient, and to monitor the efficacy of a treatment.

The invention differs from traditional endometrial cancer diagnostic and classification techniques with respect to the speed, simplicity, and reproducibility of the cancer diagnostic assay. The invention also presents targets for drug development because it identifies genes that are differentially expressed in outcome endometrial tumors, which can be utilized in the development of drugs to treat such tumors, e.g., by reducing expression of the genes or reducing activity of proteins encoded by the genes.

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The invention simplifies prognosis determination by providing an identified set of genes whose expression in endometrial cancers predicts clinical outcome as defined by tumor metastasis, recurrence, or death. In the invention RNA expression phenotyping was performed using high density microarrays generated from quantitative expression data on over 5000 (estimated 5800) genes, which have been analyzed to identify 50 specific probe sets (genes). The expression gene set has multifold uses including, but not limited to, the following examples. The expression gene set may be used as a prognostic tool for endometrial cancer patients, to make possible more finely tuned diagnosis of endometrial cancer and allow healthcare professionals to tailor treatment to individual patients' needs. The invention can also assess the efficacy of endometrial cancer treatment by determining progression or regression of endometrial cancer in patients before, during, and after endometrial cancer treatment. Another utility of the expression gene set is in the biotechnology and pharmaceutical industries' research on disease pathway discovery for therapeutic targeting. The invention can identify alterations in gene expression in endometrial cancer and can also be used to uncover and test candidate pharmaceutical agents to treat endometrial cancer.

As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat, or rodent. In all embodiments human subjects are preferred. Preferably the subject is a human either suspected of having endometrial cancer, or having been diagnosed with endometrial cancer. In a preferred embodiment of the invention the cancer is endometrioid endometrial adenocarcinoma. Methods for identifying subjects suspected of having endometrial cancer may include physical examination, subject's family medical history, subject's medical history, endometrial biopsy, or a number of imaging technologies such as ultrasonography, computed tomography, magnetic resonance imaging, magnetic resonance spectroscopy, or positron emission tomography. Diagnostic methods for endometrial cancer and the clinical delineation of endometrial cancer diagnoses are well known to those of skill in the medical arts.

As used herein, endometrial tissue sample is tissue obtained from an endometrial tissue biopsy using methods well known to those of ordinary skill in the related medical arts. The phrase "suspected of being cancerous" as used herein means an endometrial cancer tissue sample believed by one of ordinary skill in the medical arts to contain cancerous cells. Methods for obtaining the sample from the biopsy include gross apportioning of a mass, microdissection, laser-based microdissection, cytologic sampling of the endometrium using a brush, aspiration curettage, fractional dilation and curettage, or other art-known cell-separation methods.

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Because of the variability of the cell types in diseased-tissue biopsy material, and the variability in sensitivity of the diagnostic methods used, the sample size required for analysis may range from 1, 10, 50, 100, 200, 300, 500, 1000, 5000, 10,000, to 50,000 or more cells. The appropriate sample size may be determined based on the cellular composition and condition of the biopsy and the standard preparative steps for this determination and subsequent isolation of the nucleic acid for use in the invention are well known to one of ordinary skill in the art. An example of this, although not intended to be limiting, is that in some instances a sample from the biopsy may be sufficient for assessment of RNA expression without amplification, but in other instances the lack of suitable cells in a small biopsy region may require use of RNA conversion and/or amplification methods or other methods to enhance resolution of the nucleic acid molecules. Such methods, which allow use of limited biopsy materials, are well known to those of ordinary skill in the art and include, but are not limited to: direct RNA amplification, reverse transcription of RNA to cDNA, amplification of cDNA, or the generation of radio-labeled nucleic acids.

As used herein, the phrase “determining the expression of a set of nucleic acid molecules in the endometrial tissue” means identifying RNA transcripts in the tissue sample by analysis of nucleic acid or protein expression in the tissue sample. As used herein, “set” refers to a group of nucleic acid molecules that include 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 different nucleic acid sequences from the group of nucleic acid sequences numbered 1 through 50 in Table 1 (SEQ ID NOs: 1-50).

The expression of the set of nucleic acid molecules in the sample from the endometrial cancer patient can be compared to the expression of the set of nucleic acid molecules in a sample of endometrial tissue that is non-cancerous. As used herein, non-cancerous endometrial tissue means tissue determined by one of ordinary skill in the medical art to have no evidence of endometrial cancer based on standard diagnostic methods including, but not limited to, histologic staining and microscopic analysis.

Nucleic acid markers for cancer are nucleic acid molecules that by their presence or absence indicate the presence of absence of endometrial cancer. In tissue, certain nucleic acid molecules are expressed at different levels depending on whether tissue is non-cancerous or cancerous.

Hybridization methods for nucleic acids are well known to those of ordinary skill in the art (see, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York). The nucleic acid molecules from an endometrial cancer tissue sample hybridize under stringent conditions to nucleic acid markers expressed in endometrial cancer. In one embodiment the markers are sets of two or more of the nucleic acid molecules as set forth in SEQ ID NOs: 1 through 50.

The endometrial cancer nucleic acid markers disclosed herein are known genes and fragments thereof. It may be desirable to identify variants of those genes, such as allelic variants or single nucleotide polymorphisms (SNPs) in tissues. Accordingly, methods for identifying endometrial cancer nucleic acid markers, including variants of the disclosed full-length cDNAs, genomic DNAs, and SNPs are also included in the invention. The methods include contacting a nucleic acid sample (such as a cDNA library, genomic library, genomic DNA isolate, etc.) with a nucleic acid probe or primer derived from one of SEQ ID NOs:1-50. The nucleic acid sample and the probe or primer hybridize to complementary nucleotide sequences of nucleic acids in the sample, if any are present, allowing detection of nucleic acids related to SEQ ID NOs: 1-50. Preferably the probe or primer is detectably labeled. The specific conditions, reagents, and the like can be selected by one of ordinary skill in the art to selectively identify nucleic acids related to sets of two or more of SEQ ID NOs:1 through 50. The isolated nucleic acid molecule can be sequenced according to standard procedures.

In addition to native nucleic acid markers (SEQ ID NOs:1-50), the invention also includes degenerate nucleic acids that include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT, and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Similarly, nucleotide sequence triplets that encode other amino acid residues include, but are not limited to: CCA, CCC, CCG, and CCT (proline codons); CGA, CGC, CGG, CGT, AGA, and AGG (arginine codons); ACA, ACC, ACG, and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC, and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus, the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

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The invention also provides modified nucleic acid molecules, which include additions, substitutions, and deletions of one or more nucleotides such as the allelic variants and SNPs described above. In preferred embodiments, these modified nucleic acid molecules and/or the polypeptides they encode retain at least one activity or function of the unmodified nucleic acid molecule and/or the polypeptides, such as hybridization, antibody binding, etc. In certain embodiments, the modified nucleic acid molecules encode modified polypeptides, preferably polypeptides having conservative amino acid substitutions. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D. The modified nucleic acid molecules are structurally related to the unmodified nucleic acid molecules and in preferred embodiments are sufficiently structurally related to the unmodified nucleic acid molecules so that the modified and unmodified nucleic acid molecules hybridize under stringent conditions known to one of skill in the art.

For example, modified nucleic acid molecules that encode polypeptides having single amino acid changes can be prepared for use in the methods and products disclosed herein. Each of these nucleic acid molecules can have one, two, or three nucleotide substitutions exclusive of nucleotide changes corresponding to the degeneracy of the genetic code as described herein. Likewise, modified nucleic acid molecules that encode polypeptides having two amino acid changes can be prepared, which have, e.g., 2-6 nucleotide changes. Numerous modified nucleic acid molecules like these will be readily envisioned by one of skill in the art, including for example, substitutions of nucleotides in codons encoding amino acids 2 and 3, 2 and 4, 2 and 5, 2 and 6, and so on. In the foregoing example, each combination of two amino acids is included in the set of modified nucleic acid molecules, as well as all nucleotide substitutions that code for the amino acid substitutions. Additional nucleic acid molecules that encode polypeptides having additional substitutions (i.e., 3 or more), additions or deletions [e.g., by introduction of a stop codon or a splice site(s)] also can be prepared and are embraced by the invention as readily envisioned by one of ordinary skill in the art. Any of the foregoing nucleic acids can be tested by routine experimentation for retention of structural relation to or activity similar to the nucleic acids disclosed herein.

In the invention, standard hybridization techniques of microarray technology are utilized to assess patterns of nucleic acid expression and identify nucleic acid marker expression. Microarray technology, which is also known by other names including: DNA chip technology, gene chip technology, and solid-phase nucleic acid array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified nucleic acid probes on a fixed substrate, labeling target molecules with reporter molecules (e.g., radioactive, chemiluminescent, or fluorescent tags such as fluorescein, Cy3-dUTP, or Cy5-dUTP), hybridizing target nucleic acids to the probes, and evaluating target-probe hybridization. A probe with a nucleic acid sequence that perfectly matches the target sequence will, in general, result in detection of a stronger reporter-molecule signal than will probes with less perfect matches. Many components and techniques utilized in nucleic acid microarray technology are presented in *The Chipping Forecast*, Nature Genetics, Vol.21, Jan 1999, the entire contents of which is incorporated by reference herein.

According to the present invention, microarray substrates may include but are not limited to glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. In all embodiments a glass substrate is preferred. According to the invention, probes are selected from the group of nucleic acids including, but not limited to: DNA, genomic DNA, cDNA, and oligonucleotides; and may be natural or synthetic. Oligonucleotide probes preferably are 20 to 25-mer oligonucleotides and DNA/cDNA probes preferably are 500 to 5000 bases in length, although other lengths may be used. Appropriate probe length may be determined by one of ordinary skill in the art by following art-known procedures. In one embodiment, preferred probes are sets of two or more of the nucleic acid molecules set forth as SEQ ID NO: 1 through 50 (see also Table 1). Probes may be purified to remove contaminants using standard methods known to those of ordinary skill in the art such as gel filtration or precipitation.

In one embodiment, the microarray substrate may be coated with a compound to enhance synthesis of the probe on the substrate. Such compounds include, but are not limited to, oligoethylene glycols. In another embodiment, coupling agents or groups on the substrate can be used to covalently link the first nucleotide or oligonucleotide to the substrate. These agents or groups may include, but are not limited to: amino, hydroxy, bromo, and carboxy groups. These reactive groups are preferably attached to the substrate through a hydrocarbyl radical such as an alkylene or phenylene divalent radical, one valence position occupied by the chain bonding and

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the remaining attached to the reactive groups. These hydrocarbyl groups may contain up to about ten carbon atoms, preferably up to about six carbon atoms. Alkylene radicals are usually preferred containing two to four carbon atoms in the principal chain. These and additional details of the process are disclosed, for example, in U.S. Patent 4,458,066, which is incorporated by reference in its entirety.

In one embodiment, probes are synthesized directly on the substrate in a predetermined grid pattern using methods such as light-directed chemical synthesis, photochemical deprotection, or delivery of nucleotide precursors to the substrate and subsequent probe production.

In another embodiment, the substrate may be coated with a compound to enhance binding of the probe to the substrate. Such compounds include, but are not limited to: polylysine, amino silanes, amino-reactive silanes (Chipping Forecast, 1999) or chromium (Gwynne and Page, 2000). In this embodiment, presynthesized probes are applied to the substrate in a precise, predetermined volume and grid pattern, utilizing a computer-controlled robot to apply probe to the substrate in a contact-printing manner or in a non-contact manner such as ink jet or piezo-electric delivery. Probes may be covalently linked to the substrate with methods that include, but are not limited to, UV-irradiation. In another embodiment probes are linked to the substrate with heat.

Targets are nucleic acids selected from the group, including but not limited to: DNA, genomic DNA, cDNA, RNA, mRNA and may be natural or synthetic. In all embodiments, nucleic acid molecules from human endometrial tissue are preferred. The tissue may be obtained from a subject or may be grown in culture (e.g. from a endometrial cancer cell line).

In embodiments of the invention one or more control nucleic acid molecules are attached to the substrate. Preferably, control nucleic acid molecules allow determination of factors including but not limited to: nucleic acid quality and binding characteristics; reagent quality and effectiveness; hybridization success; and analysis thresholds and success. Control nucleic acids may include but are not limited to expression products of genes such as housekeeping genes or fragments thereof.

To select a set of tumor markers, the expression data generated by, for example, microarray analysis of gene expression, preferably is analyzed to determine which genes in different groups of cancer tissues are significantly differentially expressed. In the methods disclosed herein, the significance of gene expression was determined using Permax computer

software, although any standard statistical package that can discriminate significant differences in expression may be used. Permax performs permutation 2-sample t-tests on large arrays of data. For high dimensional vectors of observations, the Permax software computes t-statistics for each attribute, and assesses significance using the permutation distribution of the maximum and minimum overall attributes.

In one embodiment of the invention, expression of nucleic acid markers is used to select clinical treatment paradigms for endometrial cancer. Treatment options, as described herein, may include but are not limited to: radiotherapy, chemotherapy, adjuvant therapy, or any combination of the aforementioned methods. Aspects of treatment that may vary include, but are not limited to: dosages, timing of administration, or duration of therapy; and may or may not be combined with other treatments, which may also vary in dosage, timing, or duration. Another treatment for endometrial cancer is surgery, which can be utilized either alone or in combination with any of the aforementioned treatment methods. One of ordinary skill in the medical arts may determine an appropriate treatment paradigm based on evaluation of differential expression of sets of two or more of the nucleic acid targets set forth as SEQ ID NOs:1-50. Cancers that express markers that are indicative of a more aggressive cancer or poor prognosis may be treated with more aggressive therapies.

Progression or regression of endometrial cancer is determined by comparison of two or more different endometrial cancer tissue samples taken at two or more different times from a subject. For example, progression or regression may be evaluated by assessments of expression of sets of two or more of the nucleic acid targets, including but not limited to SEQ ID NOs:1-50, in an endometrial cancer tissue sample from a subject before, during, and following treatment for endometrial cancer.

In another embodiment, novel pharmacological agents useful in the treatment of endometrial cancer can be identified by assessing variations in the expression of sets of two or more endometrial cancer nucleic acid markers, from among SEQ ID NOs:1-50, prior to and after contacting endometrial cancer cells or tissues with candidate pharmacological agents for the treatment of endometrial cancer. The cells may be grown in culture (e.g. from an endometrial cancer cell line), or may be obtained from a subject, (e.g. in a clinical trial of candidate pharmaceutical agents to treat endometrial cancer). Alterations in expression of two or more sets of endometrial cancer nucleic acid markers, from among SEQ ID NOs:1-50, in endometrial cancer cells or tissues tested before and after contact with a candidate pharmacological agent to

treat endometrial cancer, indicate progression, regression, or stasis of the endometrial cancer thereby indicating efficacy of candidate agents and concomitant identification of lead compounds for therapeutic use in endometrial cancer.

The invention further provides efficient methods of identifying pharmacological agents or lead compounds for agents active at the level of endometrial cancer cellular function. Generally, the screening methods involve assaying for compounds that beneficially alter endometrial cancer nucleic acid molecule expression. Such methods are adaptable to automated, high-throughput screening of compounds.

The assay mixture comprises a candidate pharmacological agent. Typically, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a different response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration of agent or at a concentration of agent below the limits of assay detection. Candidate agents encompass numerous chemical classes, although typically they are organic compounds. Preferably, the candidate pharmacological agents are small organic compounds, i.e., those having a molecular weight of more than 50 yet less than about 2500, preferably less than about 1000 and, more preferably, less than about 500. Candidate agents comprise functional chemical groups necessary for structural interactions with polypeptides and/or nucleic acids, and typically include at least an amine, carbonyl, hydroxyl, or carboxyl group, preferably at least two of the functional chemical groups and more preferably at least three of the functional chemical groups. The candidate agents can comprise cyclic carbon or heterocyclic structure and/or aromatic or polyaromatic structures substituted with one or more of the above-identified functional groups. Candidate agents also can be biomolecules such as peptides, saccharides, fatty acids, sterols, isoprenoids, purines, pyrimidines, derivatives or structural analogs of the above, or combinations thereof and the like. Where the agent is a nucleic acid, the agent typically is a DNA or RNA molecule, although modified nucleic acids as defined herein are also contemplated.

Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides, synthetic organic combinatorial libraries, phage display libraries of random peptides, and the like. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant, and animal extracts are available or readily produced.

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Additionally, natural and synthetically produced libraries and compounds can be readily be modified through conventional chemical, physical, and biochemical means. Further, known pharmacological agents may be subjected to directed or random chemical modifications such as acylation, alkylation, esterification, amidification, etc. to produce structural analogs of the agents.

A variety of other reagents also can be included in the mixture. These include reagents such as salts, buffers, neutral proteins (e.g., albumin), detergents, etc. which may be used to facilitate optimal protein-protein and/or protein-nucleic acid binding. Such a reagent may also reduce non-specific or background interactions of the reaction components. Other reagents that improve the efficiency of the assay such as protease, inhibitors, nuclease inhibitors, antimicrobial agents, and the like may also be used.

The mixture of the foregoing assay materials is incubated under conditions whereby, the anti-endometrial cancer candidate agent specifically binds the cellular binding target, a portion thereof or analog thereof. The order of addition of components, incubation temperature, time of incubation, and other parameters of the assay may be readily determined. Such experimentation merely involves optimization of the assay parameters, not the fundamental composition of the assay. Incubation temperatures typically are between 4°C and 40°C. Incubation times preferably are minimized to facilitate rapid, high throughput screening, and typically are between 0.1 and 10 hours.

After incubation, the presence or absence of specific binding between the anti-endometrial cancer candidate agent and one or more binding targets is detected by any convenient method available to the user. For cell-free binding type assays, a separation step is often used to separate bound from unbound components. The separation step may be accomplished in a variety of ways. Conveniently, at least one of the components is immobilized on a solid substrate, from which the unbound components may be easily separated. The solid substrate can be made of a wide variety of materials and in a wide variety of shapes, e.g., microtiter plate, microbead, dipstick, resin particle, etc. The substrate preferably is chosen to maximize signal-to-noise ratios, primarily to minimize background binding, as well as for ease of separation and cost.

Separation may be effected for example, by removing a bead or dipstick from a reservoir, emptying or diluting a reservoir such as a microtiter plate well, rinsing a bead, particle, chromatographic column or filter with a wash solution or solvent. The separation step preferably

includes multiple rinses or washes. For example, when the solid substrate is a microtiter plate, the wells may be washed several times with a washing solution, which typically includes those components of the incubation mixture that do not participate in specific bindings such as salts, buffer, detergent, non-specific protein, etc. Where the solid substrate is a magnetic bead, the beads may be washed one or more times with a washing solution and isolated using a magnet.

Detection may be effected in any convenient way for cell-based assays such as two- or three-hybrid screens. The transcript resulting from a reporter gene transcription assay of the anti-cancer agent binding to a target molecule typically encodes a directly or indirectly detectable product, e.g., β -galactosidase activity, luciferase activity, and the like. For cell-free binding assays, one of the components usually comprises, or is coupled to, a detectable label. A wide variety of labels can be used, such as those that provide direct detection (e.g., radioactivity, luminescence, optical, or electron density, etc) or indirect detection (e.g., epitope tag such as the FLAG epitope, enzyme tag such as horseradish peroxidase, etc.). The label may be bound to an anti-cancer agent binding partner, or incorporated into the structure of the binding partner.

A variety of methods may be used to detect the label, depending on the nature of the label and other assay components. For example, the label may be detected while bound to the solid substrate or subsequent to separation from the solid substrate. Labels may be directly detected through optical or electron density, radioactive emissions, nonradiative energy transfers, etc. or indirectly detected with antibody conjugates, streptavidin-biotin conjugates, etc. Methods for detecting the labels are well known in the art.

The invention provides endometrial cancer gene-specific binding agents, methods of identifying and making such agents, and their use in diagnosis, therapy and pharmaceutical development. For example, endometrial cancer gene-specific pharmacological agents are useful in a variety of diagnostic and therapeutic applications as described herein. In general, the specificity of an endometrial cancer gene binding to a binding agent is shown by binding equilibrium constants. Targets that are capable of selectively binding an endometrial cancer gene preferably have binding equilibrium constants of at least about 10^7 M^{-1} , more preferably at least about 10^8 M^{-1} , and most preferably at least about 10^9 M^{-1} . The wide variety of cell-based and cell-free assays may be used to demonstrate endometrial cancer gene-specific binding. Cell-based assays include one, two and three hybrid screens, assays in which endometrial cancer gene-mediated transcription is inhibited or increased, etc. Cell-free assays include endometrial cancer gene-protein binding assays, immunoassays, etc. Other assays useful for screening

agents which bind endometrial cancer polypeptides include fluorescence resonance energy transfer (FRET), and electrophoretic mobility shift analysis (EMSA).

In another aspect of the invention, pre- and post-treatment alterations in expression of two or more sets of endometrial cancer nucleic acid markers including, but not limited to, SEQ ID NOs:1-50 in endometrial cancer cells or tissues may be used to assess treatment parameters including, but not limited to: dosage, method of administration, timing of administration, and combination with other treatments as described herein.

Candidate pharmacological agents may include antisense oligonucleotides that selectively bind to an endometrial cancer nucleic acid marker molecule, as identified herein, to reduce the expression of the marker molecules in endometrial cancer cells and tissues. One of ordinary skill in the art can test of the effects of a reduction of expression of endometrial cancer nucleic acid marker sequences *in vivo* or *in vitro*, to determine the efficacy of one or more antisense oligonucleotides.

As used herein, the term “antisense oligonucleotide” or “antisense” describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide, which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions.

Based upon the sequences of endometrial cancer expressed nucleic acids, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases that are complementary to the target, although in certain cases modified oligonucleotides as

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short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen that are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation, or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of an endometrial cancer expressed polypeptide. Thus, the present invention also provides for antisense oligonucleotides that are complementary to the genomic DNA corresponding to endometrial cancer expressed nucleic acids. Similarly, the use of antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art-recognized methods, which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways that do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness. The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters,

alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters, and peptides.

The term “modified oligonucleotide” also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars that are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, endometrial cancer expressed nucleic acids, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term “pharmaceutically acceptable” means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term “physiologically acceptable” refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials, which are well known in the art.

Expression of endometrial cancer nucleic acid molecules can also be determined using protein measurement methods to determine expression of SEQ ID NOs:1-50, e.g., by determining the expression of polypeptides encoded by SEQ ID NOs:1-50 (SEQ ID NOs: 51-100). Preferred methods of specifically and quantitatively measuring proteins include, but are not limited to: mass spectroscopy-based methods such as surface enhanced laser desorption ionization (SELDI; e.g., Ciphergen ProteinChip System), non-mass spectroscopy-based methods, and immunohistochemistry-based methods such as 2-dimensional gel electrophoresis.

SELDI methodology may, through procedures known to those of ordinary skill in the art, be used to vaporize microscopic amounts of tumor protein and to create a “fingerprint” of

individual proteins, thereby allowing simultaneous measurement of the abundance of many proteins in a single sample. Preferably SELDI-based assays may be utilized to classify endometrial cancer tumors. Such assays preferably include, but are not limited to the following examples. Gene products discovered by RNA microarrays may be selectively measured by specific (antibody mediated) capture to the SELDI protein disc (e.g., selective SELDI). Gene products discovered by protein screening (e.g., with 2-D gels), may be resolved by "total protein SELDI" optimized to visualize those particular markers of interest from among SEQ ID NOs:1-50. Predictive models of tumor classification from SELDI measurement of multiple markers from among SEQ ID NOs:1-50 may be utilized for the SELDI strategies. In an additional embodiment a set of endometrioid endometrial adenocarcinoma tissues may be preferably utilized to determine the risk classification of endometrial cancer based on SELDI results.

The invention also involves agents such as polypeptides that bind to endometrial cancer-associated polypeptides, i.e., SEQ ID NOs:51-100. Such binding agents can be used, for example, in screening assays to detect the presence or absence of endometrial cancer-associated polypeptides and complexes of endometrial cancer-associated polypeptides and their binding partners and in purification protocols to isolate endometrial cancer-associated polypeptides and complexes of endometrial cancer-associated polypeptides and their binding partners. Such agents also may be used to inhibit the native activity of the endometrial cancer-associated polypeptides, for example, by binding to such polypeptides.

The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to endometrial cancer-associated polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')₂ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced

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without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. See, e.g., U.S. patents 4,816,567, 5,225,539, 5,585,089, 5,693,762 and 5,859,205.

Fully human monoclonal antibodies also can be prepared by immunizing mice transgenic for large portions of human immunoglobulin heavy and light chain loci. Following immunization of these mice (e.g., XenoMouse (Abgenix), HuMAb mice (Medarex/GenPharm)), monoclonal antibodies can be prepared according to standard hybridoma technology. These monoclonal antibodies will have human immunoglobulin amino acid sequences and therefore will not provoke human anti-mouse antibody (HAMA) responses when administered to humans.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')₂, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric F(ab')₂ fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1

and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to polypeptides selected from SEQ ID NOs:51-100, and complexes of both endometrial cancer-associated polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the endometrial cancer-associated polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the endometrial cancer-associated polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the endometrial cancer-associated polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the endometrial cancer-associated polypeptides.

Thus, the endometrial cancer-associated polypeptides of the invention, including fragments thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the endometrial cancer-associated polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of endometrial cancer-associated polypeptides and for other purposes that will be apparent to those of ordinary skill in the art. For

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example, isolated endometrial cancer-associated polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, a filter, or an array substrate), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner that can interact with endometrial cancer-associated polypeptides is present in the solution, then it will bind to the substrate-endometrial cancer-associated polypeptide. The binding partner then may be isolated.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example, to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express endometrial cancer-associated polypeptides or to therapeutically useful agents according to standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium.

The invention further includes protein microarrays for analyzing expression of endometrial cancer-associated peptides selected from SEQ ID NOs:51-100. In this aspect of the invention, standard techniques of microarray technology are utilized to assess expression of the endometrial cancer-associated polypeptides and/or identify biological constituents that bind such polypeptides. The constituents of biological samples include antibodies, lymphocytes (particularly T lymphocytes), and the like. Protein microarray technology, which is also known by other names including: protein chip technology and solid-phase protein array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified peptides or proteins on a fixed substrate, binding target molecules or biological constituents to the peptides, and evaluating such binding. See, e.g., G. MacBeath and S.L. Schreiber, "Printing Proteins as Microarrays for High-Throughput Function Determination," *Science* 289(5485):1760-1763, 2000.

Preferably antibodies or antigen binding fragments thereof that specifically bind polypeptides selected from the group consisting of SEQ ID NOs:51-100 are attached to the microarray substrate in accordance with standard attachment methods known in the art. These arrays can be used to quantify the expression of the polypeptides identified herein.

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In some embodiments of the invention, one or more control peptide or protein molecules are attached to the substrate. Preferably, control peptide or protein molecules allow determination of factors such as peptide or protein quality and binding characteristics, reagent quality and effectiveness, hybridization success, and analysis thresholds and success.

The use of such methods to determine expression of endometrial cancer nucleic acids from among SEQ ID NOs:1-50 and/or proteins from among SEQ ID Nos:51-100 can be done with routine methods known to those of ordinary skill in the art and the expression determined by protein measurement methods may be used as a prognostic method for selecting treatment strategies for endometrial cancer patients.

Examples

To establish a prognostic tool for designing endometrial cancer treatment regimens, expression patterns in primary endometrial cancer specimens were assessed and correlated with clinical outcome.

Tissue processing:

RNA isolated from normal cycling (proliferative, n=2; secretory, n=2) and neoplastic (endometrioid adenocarcinoma, n=10) human endometrial specimens was reverse transcribed and resultant cDNA used for *in vitro* transcriptional synthesis of fluorescently labeled nucleic acid probes according to manufacturer's instructions. Each resultant tissue-derived probe was then separately hybridized to an Affymetrix HuFL human expression array and hybridization images analyzed with Affymetrix software to generate a data matrix of named probes by quantitative expression level in each tissue.

Data Normalization:

Average differences for each sample were rescaled to sum to 3,000,000 over all genes. Then the average differences with an Affymetrix call of Absent or Marginal were set to 20, and average differences with a call of Present but with less than 20 were also set to 20. This resulted in a dataset truncated on the left tail at a value of 20, in which only genes determined to be "present" by the Affymetrix call were included as positive expression values.

Permax Test:

Standard pooled variance t-statistics comparing the 4 normal samples to the 10 tumor samples were computed separately for each gene from their log values. Log values were used because it is natural to think of differences between tissue types as a multiplicative effect or ratio increase/decrease. Only genes with at least 2 values > 20 were considered (3665 genes), since the t statistic is undefined for genes with all values = 20, and the statistic is either 1.69 or -.62 with only one value not equal to 20, regardless of the value.

The permutation distribution was used to assess the significance of t-statistics calculated for each gene in the dataset (Permax test). The customized program written in S-plus language to calculate Permax is a data analysis software tool for testing the significance of gene expression. It has been presented by Mutter, et al., 8th International Workshop on Chromosomes in Solid Tumors, Tucson, AZ, 2000; and is available online² at biowww.dfci.harvard.edu/~gray/permax.html and from Robert J. Gray, Department of Biostatistical Science, Dana-Farber Cancer Institute, 44 Binney Street Boston, MA 02115. Permax details enclosed therein are incorporated by reference herein.. In this approach all 1001 possible ways of dividing the 14 samples into two groups of sizes 4 and 10 were considered. For each of these, the t-statistics were computed for each gene. With unequal group sizes, these distributions are not symmetric, so the significance was assessed separately in each direction. To control the overall error rate, the distributions of the maximum and minimum t-statistics over the genes were used. That is, for each gene, the p-value in the direction with expression higher (lower) in normals is the proportion of permutations with the minimum (maximum) t statistic over all genes less than (greater than) or equal to the observed value for the particular gene. A test declaring as significant any genes with say $p < .50$ then guarantees that the chance of any false positives being selected is $< 50\%$.

The t statistics have a tendency to preferentially select genes with very small variances within a group. Because of this it may be appropriate to also require minimum criteria for differences between the group means. After determining the most significant genes from the t statistics, those genes with absolute differences between means < 100 , and ratios of means < 3 were identified.

Table 1 is a spreadsheet identifying 50 genes which discriminate normal cycling from malignant endometrium.

Table 1

SEQ ID NO	GeneCode	Permax GPT	Fold GPT	Delta GPT	ChrBand	NLX GPT	TX GPT	AffyProbe Set	LocusLink	GenBank	ABREV	Title (from Unigene)
1	x6235	0.042	8.9	157.3	17q21	177	20	D88213_at	314	D88213	AOC2	amine oxidase, copper containing 2 (retina-specific)
2	x4535	0.2218	11.6	344.8	19q13.1	377	32	HG162-HT3165_at	558	M76125	AXL	AXL receptor tyrosine kinase
3	x2035	0.2727	45.9	898.1	11p15.5	20	918	M91083_at	8045	M91083	C11ORF13	chromosome 11 open reading frame 13
4	x3265	0.468	10.1	1590.5	12p13	1766	175	D13639_at	894	D13639	CCND2	cyclin D2
5	x3120	0.5	8.8	446.4	16q22.1	504	57	D21255_at	1009	D21255	CDH11	cadherin 11 (OB-cadherin, osteoblast)
6	x6580	0.2587	8.9	255.1	1p21	287	32	J04177_at	1301	J04177	COL11A1	collagen, type XI, alpha 1
7	x2140	0.1938	13.3	412.2	8q23	446	33	Y11710_maf_at	7373	Y11710	COL14A1	collagen, type XIV, alpha 1; undulin
8	x1629	0.2038	8.9	158.8	2p21	179	20	U03688_at	1545	U03688	CYP1B1	cytochrome P450, subfamily I (dioxin-inducible), polypeptide 1 (glaucoma 3, primary infantile)
9	x3108	0.028	13.9	258.1	17p13.1	278	20	U83192_at	1742	U83192	DLG4	discs, large (Drosophila) homolog 4
10	x3342	0.426	6.5	3499.8	5q34	4140	640	X68277_at	1843	X68277	DUSP1	dual specificity phosphatase 1
11	x4985	0.2448	4.4	113.1	8	33	146	U15642_s_at	1875	U15642	E2F5	E2F transcription factor 5, p130-binding
12	x671	0.446	11.2	597.5	4	656	58	D11151_at	1909	D11151	EDNRA	endothelin receptor type A
13	x2341	0.2448	5.5	1078.6	8p21.1	242	1321	HG4535-HT4940_s_at	2039	U28389	EPB49	erythrocyte membrane protein band 4.9 (dema1in)
14	x2797	0.0959	25.4	489.0	16p13.3-p13.11	20	509	L76568_xpt3_f_at	2072	L76568	ERCC4	excision repair cross-complementing rodent repair deficiency, complementation group 4
15	x6244	0.3057	3.1	750.5	13q14.1-q14.2	1103	353	M13450_at	2098	M13450	ESD	esterase D/formylglutathione hydrolase
16	x2404	0.2128	8.7	245.1	Xq22	277	32	X97249_at	2491	X97249	FSHPRH1	FSH primary response (LRPR1, rat) homolog 1
17	x4516	0.3247	39.1	761.3	3p21.3	20	781	U49082_at	10991	U49082	G17	G17 transporter protein
18	x4495	0.2218	55.8	3521.2	2p12-q11	3585	64	M85276_at	10578	M85276	GNLY	granulysin
19	x1222	0.014	16.5	310.3	2q14-q21	330	20	M36284_s_at	2995	M36284	GYPC	glycophorin C (Gerbich blood group)
20	x2590	0.1359	7.5	129.1	15q22	149	20	U50078_at	8925	U50078	HERC1	hect (homologous to the E6-AP

															(UBE3A) carboxyl terminus domain and RCC1 (CHC1)-like domain (RLD) 1
21	x881	0.0599	10.3	185.2		2	205	20			U44111_at	3176	U44111	HNMT	histamine N-methyltransferase
22	x5023	0.2388	11.2	395.1	2q37.1-q36.3		434	39			X77307_at	3357	X77307	HTR2B	5-hydroxytryptamine (serotonin) receptor 2B
23	x2719	0.2108	7.9	206.0	9p22		236	30			J00212_f at	3452	V00540	IFNA21	interferon, alpha 21
24	x5442	0.1618	42.3	1454.6	12q22-q23		1490	35			X57025_at	3479	X57025	IGF1	insulin-like growth factor 1 (somatomedin C)
25	x5452	0.5	6.2	420.4	19p13.1		501	81			U61263_at	10994	U61263	ILVBL	ilvB (bacterial acetoacetate synthase)-like
26	x6197	0.1808	10.4	188.0	4q34.1-q35.1		208	20			X15949_at	3660	X15949	IRF2	interferon regulatory factor 2
27	x3700	0.3447	7.2	124.9	3q21-q25		145	20			D13626_at	9934	D13626	KIAA0001	KIAA0001 gene product
28	x1553	0.1728	3.7	3035.7	12q13		1115	4151			X12876_s at	3875	X12876	KRT18	keratin 18
29	x5912	0.0669	10.2	4816.8	12q13		521	5338			X74929_s at	3856	X74929	KRT8	keratin 8
30	x197	0.035	43.7	853.4	16q22.1		873	20			M12625_at	3931	M12625	LCAT	lecithin-cholesterol acyltransferase
31	x723	0.2478	5.8	7378.3	22q13.1		8915	1537			J04456_at	3956	J04456	LGALS1	lectin, galactoside-binding, soluble, 1 (galectin 1)
32	x1271	0.1299	3.8	1609.5	4q		583	2192			M93036_at	4072	M93036	M4S1	membrane component, chromosomal 4, surface marker (35kD glycoprotein)
33	x6752	0.431	4.0	613.2	14		818	205			Z24725_at	10979	Z24725	MIG2	mitogen inducible 2
34	x1469	0.2038	18.2	797.4	14q11-q12		844	46			Z48481_at	4323	Z48481	MMP14	matrix metalloproteinase 14 (membrane-inserted)
35	x879	0.2458	22.3	1149.7	1q43		1204	54			M30269_at	4811	M30269	NID	nidogen (enactin)
36	x1397	0.3946	11.6	724.8	5q14		793	68			HG3510-HT3704_at	7025	X12795	NR2F1	nuclear receptor subfamily 2, group F, member 1
37	x2831	0.2987	6.0	204.3	10q21.3-q23.1		41	245			M24486_s_at	5033	M24486	P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide 1
38	x2670	0.2478	158.2	4966.1	9q34		4998	32			HG721-HT4827_s_at	5047	J04129	PAEP(alt2)	progesteragen-associated endometrial protein (placental protein 14, pregnancy-associated endometrial alpha-2-globulin, alpha uterine protein); Alternate Splice 2
39	x5757	0.2038	12.3	3977.7	7q22		4331	353			L33799_at	5118	L33799	PCOLCE	procollagen C-endopeptidase enhancer

40	x6701	0.3077	17.8	1101.4	4q11-q13	1167	65	M21574_at	5156	M21574	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide
41	x6741	0.2068	5.1	120.6	Xq21-q27	150	29	D00860_at	5631	D00860	PRPS1	phosphoribosyl pyrophosphate synthetase 1
42	x1195	0.1099	10.2	183.7	Xp22.3-p22.2	204	20	Y00971_at	5634	Y00971	PRPS2	phosphoribosyl pyrophosphate synthetase 2
43	x5284	0.0789	11.6	212.7	4p15.31	233	20	M16447_at	5860	M16447	QDPR	quinoid dihydropteridine reductase
44	x320	0.4076	5.6	167.7	1p31-p22	204	37	X98001_at	5876	X98001	RABGGTB	Rab geranylgeranyltransferase, beta subunit
45	x6986	0.3417	13.9	628.3	10q11.1	677	49	L36033_at	6387	L36033	SDF1	stromal cell-derived factor 1
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47	x4685	0.2218	8.3	215.8	Xq28	245	30	X92396_at	6845	X92396	SYBL1	synaptobrevin-like 1
48	x5624	0.2228	3.1	666.3	15q13	988	321	L14837_at	7082	L14837	TJP1	tight junction protein 1 (zona occludens 1)
49	x4880	0.038	13.0	239.8	11p13	260	20	X69950_s at	51352	X69950	WTT-1	Wilms tumor associated protein
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Key:

SEQ ID NO

GeneCode

PermaxGPT

FoldGPT

DeltaGPT

ChrBand

NLXGPT

TXGPT

Sequence identifier number

Internal lab unique identifier, numbers preceded by an "x"

Permax value using GPT dataset

Ratio of NLXGPT to TXGPT, inverted if needed to yield value >1

Arithmetic difference of NLXGPT and TXGPT, absolute value

Karyotypic locus of gene

Mean expression in GPT units of 4 normal endometria

Mean expression in GPT units of 10 endometrioid endometrial

adenocarcinomas

Affymetrix probe identifier in HuFL human expression array chip

LocusLink ID number, when available.

The GenBank entry for sequence used by Affymetrix to design probes

When in full caps, this is the LocusLink recommended nomenclature.

Text description of gene. Usually LocusLink label

AffyProbeSet

LocusLink

GenBank

Abrev

Title

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The present invention is not limited in scope by the examples provided, since the examples are intended as illustrations of various aspects of the invention and other functionally equivalent embodiments are within the scope of the invention. Various
5 modifications of the invention in addition to those shown are described herein will become apparent to those skilled in the art for the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.

All references, patents, and patent publications that are recited in this application are
10 incorporated in their entirety herein by reference.

I claim:

Claims

1. A method for diagnosing endometrial cancer in a subject suspected of having endometrial cancer comprising:
 - 5 obtaining from the subject an endometrial tissue sample suspected of being cancerous, determining the expression of a set of nucleic acid molecules or expression products thereof in the endometrial tissue sample, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
- 10 2. The method of claim 1, wherein the set of nucleic acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
3. The method of claim 1, wherein the set includes at least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
- 15 4. The method of claim 1, wherein the set includes at least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
5. The method of claim 1, wherein the set includes at least 10 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
- 20 6. The method of claim 1, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
- 25 7. The method of claim 1, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
8. The method of claim 1, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.
- 30 9. The method of claim 1, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

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10. The method of claim 1, further comprising:

determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the endometrial tissue sample suspected of being cancerous and the non-cancerous endometrial tissue sample.

11. A method for selecting a course of treatment of a subject having or suspected of having endometrial cancer, comprising:

obtaining from the subject an endometrial tissue sample suspected of being cancerous, determining the expression of a set of nucleic acid markers or expression products thereof which are differentially expressed in endometrial tumor tissue samples, and selecting a course of treatment appropriate to the endometrial cancer of the subject.

12. The method of claim 11 wherein the endometrial cancer is endometrioid endometrial carcinoma.

13. The method of claim 12, further comprising:

determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample.

14. The method of claim 11, wherein the expression of a set of nucleic acid markers is determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

15. The method of claim 14, wherein the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array.

16. A method for evaluating treatment of endometrial cancer, comprising:

obtaining a first determination of the expression of a set of nucleic acid molecules, or expression products thereof, which are differentially expressed in an endometrial tumor tissue sample from a subject undergoing treatment for cancer,

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obtaining a second determination of the expression of a set of nucleic acid molecules, or expression products thereof, which are differentially expressed in a second endometrial tumor tissue sample from the subject after obtaining the first determination,

comparing the first determination of expression to the second determination of
5 expression as an indication of evaluation of the treatment.

17. The method of claim 16, wherein the cancer is endometrioid endometrial adenocarcinoma.

10 18. The method of claim 17, further comprising:
determining the expression of a set of nucleic acid markers which are differentially expressed in non-cancerous endometrial tissue samples.

19. The method of claim 16, wherein the expression of a set of nucleic acid markers is
15 determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

20. The method of claim 16, wherein the nucleic acid hybridization is performed using a
solid-phase nucleic acid molecule array.

20 21. A solid-phase nucleic acid molecule array consisting essentially of at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50 fixed to a solid substrate.

25 22. The solid-phase nucleic acid molecule array of claim 21, further comprising at least one control nucleic acid molecule.

23. The solid-phase nucleic acid molecule array of claim 21, wherein the set of nucleic acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting
30 of SEQ ID NOs:1-50.

24. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

25. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

5 26. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 10 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

27. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

10

28. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

29. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

15

30. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

20 31. The solid-phase nucleic acid molecule array of claim 21, wherein the solid substrate comprises a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon.

25 32. The solid-phase nucleic acid molecule array of claim 21, wherein the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

33. A solid-phase protein microarray comprising at least two antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate.

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34. The protein microarray of claim 33, wherein the microarray further comprises an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100.

5 35. The protein microarray of claim 34, wherein the cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs: 51-100 is a endometrial cancer associated polypeptide.

36. The protein microarray of claim 33, further comprising at least one control
10 polypeptide molecule.

37. The protein microarray of claim 33, wherein the antibodies are monoclonal or polyclonal antibodies.

15 38. The protein microarray of claim 33, wherein the antibodies are chimeric, human, or humanized antibodies.

39. The protein microarray of claim 33, wherein the antibodies are single chain
20 antibodies.

40. The protein microarray of claim 33, wherein the antigen-binding fragments are F(ab')₂, Fab, Fd, or Fv fragments.

41. A method for identifying lead compounds for a pharmacological agent useful in the
25 treatment of endometrial cancer, comprising:

contacting a endometrial cancer cell or tissue with a candidate pharmacological agent,
determining the expression of a set of nucleic acid molecules in the endometrial
cancer cell or tissue sample under conditions which, in the absence of the candidate
pharmacological agent, permit a first amount of expression of the set of nucleic acid
30 molecules wherein the set of nucleic acid molecules comprises at least two nucleic acid
molecules selected from the group consisting of SEQ ID NOs:1-50, and

detecting a test amount of the expression of the set of nucleic acid molecules, wherein
a decrease in the test amount of expression in the presence of the candidate pharmacological

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agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which is useful in the treatment of endometrial cancer.

- 5 42. The method of claim 41, wherein the set of nucleic acid molecules is differentially expressed in endometrioid endometrial tumor tissue samples.

- 1 -

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<211> 507
<212> DNA
<213> Homo sapiens

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 <211> 672
 <212> DNA
 <213> Homo sapiens

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<221> Unsure

<222> (2746) .. (2746)

<223> n = a, c, g or t/u

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aaaaaaaaa aaaaaaa

3437

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<211> 4898

<212> DNA

<213> Homo sapiens

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		675					680					685				
Pro	Gly	Ser	Val	Tyr	Phe	Glu	Lys	Gly	Gln	Asp	Ala	Gly	Leu	Cys	Ser	
	690					695					700					

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Ile Asn Pro Val Ala Cys Leu Pro Asp Leu Ala Ala Cys Val Pro Asp
 705 710 715 720

Leu Pro Pro Phe Ser Tyr His Gly Phe
 725

<210> 52
 <211> 885
 <212> PRT
 <213> Homo sapiens

<400> 52

Met Ala Trp Arg Cys Pro Arg Met Gly Arg Val Pro Leu Ala Trp Cys
 1 5 10 15

Leu Ala Leu Cys Gly Trp Ala Cys Met Ala Pro Arg Gly Thr Gln Ala
 20 25 30

Glu Glu Ser Pro Phe Val Gly Asn Pro Gly Asn Ile Thr Gly Ala Arg
 35 40 45

Gly Leu Thr Gly Thr Leu Arg Cys Gln Leu Gln Val Gln Gly Glu Pro
 50 55 60

Pro Glu Val His Trp Leu Arg Asp Gly Gln Ile Leu Glu Leu Ala Asp
 65 70 75 80

Ser Thr Gln Thr Gln Val Pro Leu Gly Glu Asp Glu Gln Asp Asp Trp
 85 90 95

Ile Val Val Ser Gln Leu Arg Ile Thr Ser Leu Gln Leu Ser Asp Thr
 100 105 110

Gly Gln Tyr Gln Cys Leu Val Phe Leu Gly His Gln Thr Phe Val Ser
 115 120 125

Gln Pro Gly Tyr Val Gly Leu Glu Gly Leu Pro Tyr Phe Leu Glu Glu
 130 135 140

Pro Glu Asp Arg Thr Val Ala Ala Asn Thr Pro Phe Asn Leu Ser Cys
 145 150 155 160

Gln Ala Gln Gly Pro Pro Glu Pro Val Asp Leu Leu Trp Leu Gln Asp
 165 170 175

Ala Val Pro Leu Ala Thr Ala Pro Gly His Gly Pro Gln Arg Ser Leu
 180 185 190

His Val Pro Gly Leu Asn Lys Thr Ser Ser Phe Ser Cys Glu Ala His
 195 200 205

Asn Ala Lys Gly Val Thr Thr Ser Arg Thr Ala Thr Ile Thr Val Leu
 210 215 220

Pro Gln Gln Pro Arg Asn Leu His Leu Val Ser Arg Gln Pro Thr Glu
 225 230 235 240

Leu Glu Val Ala Trp Thr Pro Gly Leu Ser Gly Ile Tyr Pro Leu Thr
 245 250 255

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His Cys Thr Leu Gln Ala Val Leu Ser Asp Asp Gly Met Gly Ile Gln
 260 265 270
 Ala Gly Glu Pro Asp Pro Pro Glu Glu Pro Leu Thr Ser Gln Ala Ser
 275 280 285
 Val Pro Pro His Gln Leu Arg Leu Gly Ser Leu His Pro His Thr Pro
 290 295 300
 Tyr His Ile Arg Val Ala Cys Thr Ser Ser Gln Gly Pro Ser Ser Trp
 305 310 315 320
 Thr His Trp Leu Pro Val Glu Thr Pro Glu Gly Val Pro Leu Gly Pro
 325 330 335
 Pro Lys Asn Ile Ser Ala Thr Arg Asn Gly Ser Gln Ala Phe Val His
 340 345 350
 Trp Gln Glu Pro Arg Ala Pro Leu Gln Gly Thr Leu Leu Gly Tyr Arg
 355 360 365
 Leu Ala Tyr Gln Gly Gln Asp Thr Pro Glu Val Leu Met Asp Ile Gly
 370 375 380
 Leu Arg Gln Glu Val Thr Leu Glu Leu Gln Gly Asp Gly Ser Val Ser
 385 390 395 400
 Asn Leu Thr Val Cys Val Ala Ala Tyr Thr Ala Ala Gly Asp Gly Pro
 405 410 415
 Trp Ser Leu Pro Val Pro Leu Glu Ala Trp Arg Pro Val Lys Glu Pro
 420 425 430
 Ser Thr Pro Ala Phe Ser Trp Pro Trp Trp Tyr Val Leu Leu Gly Ala
 435 440 445
 Val Val Ala Ala Ala Cys Val Leu Ile Leu Ala Leu Phe Leu Val His
 450 455 460
 Arg Arg Lys Lys Glu Thr Arg Tyr Gly Glu Val Phe Glu Pro Thr Val
 465 470 475 480
 Glu Arg Gly Glu Leu Val Val Arg Tyr Arg Val Arg Lys Ser Tyr Ser
 485 490 495
 Arg Arg Thr Thr Glu Ala Thr Leu Asn Ser Leu Gly Ile Ser Glu Glu
 500 505 510
 Leu Lys Glu Lys Leu Arg Asp Val Met Val Asp Arg His Lys Val Ala
 515 520 525
 Leu Gly Lys Thr Leu Gly Glu Gly Glu Phe Gly Ala Val Met Glu Gly
 530 535 540
 Gln Leu Asn Gln Asp Asp Ser Ile Leu Lys Val Ala Val Lys Thr Met
 545 550 555 560
 Lys Ile Ala Ile Cys Thr Arg Ser Glu Leu Glu Asp Phe Leu Ser Glu
 565 570 575

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Ala Val Cys Met Lys Glu Phe Asp His Pro Asn Val Met Arg Leu Ile
 580 585 590
 Gly Val Cys Phe Gln Gly Ser Glu Arg Glu Ser Phe Pro Ala Pro Val
 595 600 605
 Val Ile Leu Pro Phe Met Lys His Gly Asp Leu His Ser Phe Leu Leu
 610 615 620
 Tyr Ser Arg Leu Gly Asp Gln Pro Val Tyr Leu Pro Thr Gln Met Leu
 625 630 635 640
 Val Lys Phe Met Ala Asp Ile Ala Ser Gly Met Glu Tyr Leu Ser Thr
 645 650 655
 Lys Arg Phe Ile His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Asn
 660 665 670
 Glu Asn Met Ser Val Cys Val Ala Asp Phe Gly Leu Ser Lys Lys Ile
 675 680 685
 Tyr Asn Gly Asp Tyr Tyr Arg Gln Gly Arg Ile Ala Lys Met Pro Val
 690 695 700
 Lys Trp Ile Ala Ile Glu Ser Leu Ala Asp Arg Val Tyr Thr Ser Lys
 705 710 715 720
 Ser Asp Val Trp Ser Phe Gly Val Thr Met Trp Glu Ile Ala Thr Arg
 725 730 735
 Gly Gln Thr Pro Tyr Pro Gly Val Glu Asn Ser Glu Ile Tyr Asp Tyr
 740 745 750
 Leu Arg Gln Gly Asn Arg Leu Lys Gln Pro Ala Asp Cys Leu Asp Gly
 755 760 765
 Leu Tyr Ala Leu Met Ser Arg Cys Trp Glu Leu Asn Pro Gln Asp Arg
 770 775 780
 Pro Ser Phe Thr Glu Leu Arg Glu Asp Leu Glu Asn Thr Leu Lys Ala
 785 790 795 800
 Leu Pro Pro Ala Gln Glu Pro Asp Glu Ile Leu Tyr Val Asn Met Asp
 805 810 815
 Glu Gly Gly Gly Tyr Pro Glu Pro Pro Gly Ala Ala Gly Gly Ala Asp
 820 825 830
 Pro Pro Thr Gln Pro Asp Pro Lys Asp Ser Cys Ser Cys Leu Thr Ala
 835 840 845
 Ala Glu Val His Pro Ala Gly Arg Tyr Val Leu Cys Pro Ser Thr Thr
 850 855 860
 Pro Ser Pro Ala Gln Pro Ala Asp Arg Gly Ser Pro Ala Ala Pro Gly
 865 870 875 880
 Gln Glu Asp Gly Ala
 885

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<210> 53
 <211> 373
 <212> PRT
 <213> Homo sapiens

<400> 53

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Met Leu Leu Gly Leu Ala Ala Met Glu Leu Lys Val Trp Val Asp Gly
1          5          10          15

Ile Gln Arg Val Val Cys Gly Val Ser Glu Gln Thr Thr Cys Gln Glu
          20          25          30

Val Val Ile Ala Leu Ala Gln Ala Ile Gly Gln Thr Gly Arg Phe Val
          35          40          45

Leu Val Gln Arg Leu Arg Glu Lys Glu Arg Gln Leu Leu Pro Gln Glu
          50          55          60

Cys Pro Val Gly Ala Gln Ala Thr Cys Gly Gln Phe Ala Ser Asp Val
65          70          75          80

Gln Phe Val Leu Arg Arg Thr Gly Pro Ser Leu Ala Gly Arg Pro Ser
          85          90          95

Ser Asp Ser Cys Pro Pro Pro Glu Arg Cys Leu Ile Arg Ala Ser Leu
          100          105          110

Pro Val Lys Pro Arg Ala Ala Leu Gly Cys Glu Pro Arg Lys Thr Leu
          115          120          125

Thr Pro Glu Pro Ala Pro Ser Leu Ser Arg Pro Gly Pro Ala Ala Pro
          130          135          140

Val Thr Pro Thr Pro Gly Cys Cys Thr Asp Leu Arg Gly Leu Glu Leu
145          150          155          160

Arg Val Gln Arg Asn Ala Glu Glu Leu Gly His Glu Ala Phe Trp Glu
          165          170          175

Gln Glu Leu Arg Arg Glu Gln Ala Arg Glu Arg Glu Gly Gln Ala Arg
          180          185          190

Leu Gln Ala Leu Ser Ala Ala Thr Ala Glu His Ala Ala Arg Leu Gln
          195          200          205

Ala Leu Asp Ala Gln Ala Arg Ala Leu Glu Ala Glu Leu Gln Leu Ala
          210          215          220

Ala Glu Ala Pro Gly Pro Pro Ser Pro Met Ala Ser Ala Thr Glu Arg
225          230          235          240

Leu His Gln Asp Leu Ala Val Gln Glu Arg Gln Ser Ala Glu Val Gln
          245          250          255

Gly Ser Leu Ala Leu Val Ser Arg Ala Leu Glu Ala Ala Glu Arg Ala
          260          265          270

Leu Gln Ala Gln Ala Gln Glu Leu Glu Glu Leu Asn Arg Glu Leu Arg

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275 280 285
 Gln Cys Asn Leu Gln Gln Phe Ile Gln Gln Thr Gly Ala Ala Leu Pro
 290 295 300
 Pro Pro Pro Arg Pro Asp Arg Gly Pro Pro Gly Thr Gln Gly Pro Leu
 305 310 315 320
 Pro Pro Ala Arg Glu Glu Ser Leu Leu Gly Ala Pro Ser Glu Ser His
 325 330 335
 Ala Gly Ala Gln Pro Arg Pro Arg Gly Gly Pro His Asp Ala Glu Leu
 340 345 350
 Leu Glu Val Ala Ala Ala Pro Ala Pro Glu Trp Cys Pro Leu Ala Ala
 355 360 365
 Gln Pro Gln Ala Leu
 370
 <210> 54
 <211> 289
 <212> PRT
 <213> Homo sapiens
 <400> 54
 Met Glu Leu Leu Cys His Glu Val Asp Pro Val Arg Arg Ala Val Arg
 1 5 10 15
 Asp Arg Asn Leu Leu Arg Asp Asp Arg Val Leu Gln Asn Leu Leu Thr
 20 25 30
 Ile Glu Glu Arg Tyr Leu Pro Gln Cys Ser Tyr Phe Lys Cys Val Gln
 35 40 45
 Lys Asp Ile Gln Pro Tyr Met Arg Arg Met Val Ala Thr Trp Met Leu
 50 55 60
 Glu Val Cys Glu Glu Gln Lys Cys Glu Glu Glu Val Phe Pro Leu Ala
 65 70 75 80
 Met Asn Tyr Leu Asp Arg Phe Leu Ala Gly Val Pro Thr Pro Lys Ser
 85 90 95
 His Leu Gln Leu Leu Gly Ala Val Cys Met Phe Leu Ala Ser Lys Leu
 100 105 110
 Lys Glu Thr Ser Pro Leu Thr Ala Glu Lys Leu Cys Ile Tyr Thr Asp
 115 120 125
 Asn Ser Ile Lys Pro Gln Glu Leu Leu Glu Trp Glu Leu Val Val Leu
 130 135 140
 Gly Lys Leu Lys Trp Asn Leu Ala Ala Val Thr Pro His Asp Phe Ile
 145 150 155 160
 Glu His Ile Leu Arg Lys Leu Pro Gln Gln Arg Glu Lys Leu Ser Leu
 165 170 175

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Ile Arg Lys His Ala Gln Thr Phe Ile Ala Leu Cys Ala Thr Asp Phe
 180 185 190

Lys Phe Ala Met Tyr Pro Pro Ser Met Ile Ala Thr Gly Ser Val Gly
 195 200 205

Ala Ala Ile Cys Gly Leu Gln Gln Asp Glu Glu Val Ser Ser Leu Thr
 210 215 220

Cys Asp Ala Leu Thr Glu Leu Leu Ala Lys Ile Thr Asn Thr Asp Val
 225 230 235 240

Asp Cys Leu Lys Ala Cys Gln Glu Gln Ile Glu Ala Val Leu Leu Asn
 245 250 255

Ser Leu Gln Gln Tyr Arg Gln Asp Gln Arg Asp Gly Ser Lys Ser Glu
 260 265 270

Asp Glu Leu Asp Gln Ala Ser Thr Pro Thr Asp Val Arg Asp Ile Asp
 275 280 285

Leu

<210> 55
 <211> 693
 <212> PRT
 <213> Homo sapiens

<400> 55

Met Lys Glu Asn Tyr Cys Leu Gln Ala Ala Leu Val Cys Leu Gly Met
 1 5 10 15

Leu Cys His Ser His Ala Phe Ala Pro Glu Arg Arg Gly His Leu Arg
 20 25 30

Pro Ser Phe His Gly His His Glu Lys Gly Lys Glu Gly Gln Val Leu
 35 40 45

Gln Arg Ser Lys Arg Gly Trp Val Trp Asn Gln Phe Phe Val Ile Glu
 50 55 60

Glu Tyr Thr Gly Pro Asp Pro Val Leu Val Gly Arg Leu His Ser Asp
 65 70 75 80

Ile Asp Ser Gly Asp Gly Asn Ile Lys Tyr Ile Leu Ser Gly Glu Gly
 85 90 95

Ala Gly Thr Ile Phe Val Ile Asp Asp Lys Ser Gly Asn Ile His Ala
 100 105 110

Thr Lys Thr Leu Asp Arg Glu Glu Arg Ala Gln Tyr Thr Leu Met Ala
 115 120 125

Gln Ala Val Asp Arg Asp Thr Asn Arg Pro Leu Glu Pro Pro Ser Glu
 130 135 140

Phe Ile Val Lys Val Gln Asp Ile Asn Asp Asn Pro Pro Glu Phe Leu
 145 150 155 160

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His Glu Thr Tyr His Ala Asn Val Pro Glu Arg Ser Asn Val Gly Thr
 165 170 175
 Ser Val Ile Gln Val Thr Ala Ser Asp Ala Asp Asp Pro Thr Tyr Gly
 180 185 190
 Asn Ser Ala Lys Leu Val Tyr Ser Ile Leu Glu Gly Gln Pro Tyr Phe
 195 200 205
 Ser Val Glu Ala Gln Thr Gly Ile Ile Arg Thr Ala Leu Pro Asn Met
 210 215 220
 Asp Arg Glu Ala Lys Glu Glu Tyr His Val Val Ile Gln Ala Lys Asp
 225 230 235 240
 Met Gly Gly His Met Gly Gly Leu Ser Gly Thr Thr Lys Val Thr Ile
 245 250 255
 Thr Leu Thr Asp Val Asn Asp Asn Pro Pro Lys Phe Pro Gln Ser Val
 260 265 270
 Tyr Gln Ile Ser Val Ser Glu Ala Ala Val Pro Gly Glu Glu Val Gly
 275 280 285
 Arg Val Lys Ala Lys Asp Pro Asp Ile Gly Glu Asn Gly Leu Val Thr
 290 295 300
 Tyr Asn Ile Val Asp Gly Asp Gly Met Glu Ser Phe Glu Ile Thr Thr
 305 310 315 320
 Asp Tyr Glu Thr Gln Glu Gly Val Ile Lys Leu Lys Lys Pro Val Asp
 325 330 335
 Phe Glu Thr Lys Arg Ala Tyr Ser Leu Lys Val Glu Ala Ala Asn Val
 340 345 350
 His Ile Asp Pro Lys Phe Ile Ser Asn Gly Pro Phe Lys Asp Thr Val
 355 360 365
 Thr Val Lys Ile Ala Val Glu Asp Ala Asp Glu Pro Pro Met Phe Leu
 370 375 380
 Ala Pro Ser Tyr Ile His Glu Val Gln Glu Asn Ala Ala Ala Gly¹ Thr
 385 390 395 400
 Val Val Gly Arg Val His Ala Lys Asp Pro Asp Ala Ala Asn Ser Pro
 405 410 415
 Ile Arg Tyr Ser Ile Asp Arg His Thr Asp Leu Asp Arg Phe Phe Thr
 420 425 430
 Ile Asn Pro Glu Asp Gly Phe Ile Lys Thr Thr Lys Pro Leu Asp Arg
 435 440 445
 Glu Glu Thr Ala Trp Leu Asn Ile Thr Val Phe Ala Ala Glu Ile His
 450 455 460
 Asn Arg His Gln Glu Ala Lys Val Pro Val Ala Ile Arg Val Leu Asp
 465 470 475 480

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Val Asn Asp Asn Ala Pro Lys Phe Ala Ala Pro Tyr Glu Gly Phe Ile
 485 490 495
 Cys Glu Ser Asp Gln Thr Lys Pro Leu Ser Asn Gln Pro Ile Val Thr
 500 505 510
 Ile Ser Ala Asp Asp Lys Asp Asp Thr Ala Asn Gly Pro Arg Phe Ile
 515 520 525
 Phe Ser Leu Pro Pro Glu Ile Ile His Asn Pro Asn Phe Thr Val Arg
 530 535 540
 Asp Asn Arg Asp Asn Thr Ala Gly Val Tyr Ala Arg Arg Gly Gly Phe
 545 550 555 560
 Ser Arg Gln Lys Gln Asp Leu Tyr Leu Leu Pro Ile Val Ile Ser Asp
 565 570 575
 Gly Gly Ile Pro Pro Met Ser Ser Thr Asn Thr Leu Thr Ile Lys Val
 580 585 590
 Cys Gly Cys Asp Val Asn Gly Ala Leu Leu Ser Cys Asn Ala Glu Ala
 595 600 605
 Tyr Ile Leu Asn Ala Gly Leu Ser Thr Gly Ala Leu Ile Ala Ile Leu
 610 615 620
 Ala Cys Ile Val Ile Leu Leu Gly Cys Pro Ser Leu Met Glu Pro Pro
 625 630 635 640
 Ser Pro Arg Glu Asp Met Arg Leu Leu Tyr Leu Gly Phe Gln Leu Met
 645 650 655
 Leu Phe Ser Tyr Val Lys Val Asn Arg Arg Phe Cys Leu Leu Gly Val
 660 665 670
 Phe Ile Lys Leu Pro Phe Leu Tyr Val Val Ala Thr Glu Ser Pro Thr
 675 680 685
 Thr Leu Thr Ser Leu
 690

<210> 56
 <211> 1806
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (758)..(758)
 <223> Xaa = any amino acid

<220>
 <221> UNSURE
 <222> (809)..(809)
 <223> Xaa = any amino acid

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<400> 56

Met Glu Pro Trp Ser Ser Arg Trp Lys Thr Lys Arg Trp Leu Trp Asp
 1 5 10 15
 Phe Thr Val Thr Thr Leu Ala Leu Thr Phe Leu Phe Gln Ala Arg Glu
 20 25 30
 Val Arg Gly Ala Ala Pro Val Asp Val Leu Lys Ala Leu Asp Phe His
 35 40 45
 Asn Ser Pro Glu Gly Ile Ser Lys Thr Thr Gly Phe Cys Thr Asn Arg
 50 55 60
 Lys Asn Ser Lys Gly Ser Asp Thr Ala Tyr Arg Val Ser Lys Gln Ala
 65 70 75 80
 Gln Leu Ser Ala Pro Thr Lys Gln Leu Phe Pro Gly Gly Thr Phe Pro
 85 90 95
 Glu Asp Phe Ser Ile Leu Phe Thr Val Lys Pro Lys Lys Gly Ile Gln
 100 105 110
 Ser Phe Leu Leu Ser Ile Tyr Asn Glu His Gly Ile Gln Gln Ile Gly
 115 120 125
 Val Glu Val Gly Arg Ser Pro Val Phe Leu Phe Glu Asp His Thr Gly
 130 135 140
 Lys Pro Ala Pro Glu Asp Tyr Pro Leu Phe Arg Thr Val Asn Ile Ala
 145 150 155 160
 Asp Gly Lys Trp His Arg Val Ala Ile Ser Val Glu Lys Lys Thr Val
 165 170 175
 Thr Met Ile Val Asp Cys Lys Lys Lys Thr Thr Lys Pro Leu Asp Arg
 180 185 190
 Ser Glu Arg Ala Ile Val Asp Thr Asn Gly Ile Thr Val Phe Gly Thr
 195 200 205
 Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Phe Leu
 210 215 220
 Ile Thr Gly Asp Pro Lys Ala Ala Tyr Asp Tyr Cys Glu His Tyr Ser
 225 230 235 240
 Pro Asp Cys Asp Ser Ser Ala Pro Lys Ala Ala Gln Ala Gln Glu Pro
 245 250 255
 Gln Ile Asp Glu Tyr Ala Pro Glu Asp Ile Ile Glu Tyr Asp Tyr Glu
 260 265 270
 Tyr Gly Glu Ala Glu Tyr Lys Glu Ala Glu Ser Val Thr Glu Gly Pro
 275 280 285
 Thr Val Thr Glu Glu Thr Ile Ala Gln Thr Glu Ala Asn Ile Val Asp
 290 295 300
 Asp Phe Gln Glu Tyr Asn Tyr Gly Thr Met Glu Ser Tyr Gln Thr Glu

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305		310		315		320
Ala Pro Arg His Val Ser Gly Thr Asn Glu Pro Asn Pro Val Glu Glu						
		325		330		335
Ile Phe Thr Glu Glu Tyr Leu Thr Gly Glu Asp Tyr Asp Ser Gln Arg						
		340		345		350
Lys Asn Ser Glu Asp Thr Leu Tyr Glu Asn Lys Glu Ile Asp Gly Arg						
		355		360		365
Asp Ser Asp Leu Leu Val Asp Gly Asp Leu Gly Glu Tyr Asp Phe Tyr						
		370		375		380
Glu Tyr Lys Glu Tyr Glu Asp Lys Pro Thr Ser Pro Pro Asn Glu Glu						
		385		390		400
Phe Gly Pro Gly Val Pro Ala Glu Thr Asp Ile Thr Glu Thr Ser Ile						
		405		410		415
Asn Gly His Gly Ala Tyr Gly Glu Lys Gly Gln Lys Gly Glu Pro Ala						
		420		425		430
Val Val Glu Pro Gly Met Leu Val Glu Gly Pro Pro Gly Pro Ala Gly						
		435		440		445
Pro Ala Gly Ile Met Gly Pro Pro Gly Leu Gln Gly Pro Thr Gly Pro						
		450		455		460
Pro Gly Asp Pro Gly Asp Arg Gly Pro Pro Gly Arg Pro Gly Leu Pro						
		465		470		475
Gly Ala Asp Gly Leu Pro Gly Pro Pro Gly Thr Met Leu Met Leu Pro						
		485		490		495
Phe Arg Tyr Gly Gly Asp Gly Ser Lys Gly Pro Thr Ile Ser Ala Gln						
		500		505		510
Glu Ala Gln Ala Gln Ala Ile Leu Gln Gln Ala Arg Ile Ala Leu Arg						
		515		520		525
Gly Pro Pro Gly Pro Met Gly Leu Thr Gly Arg Pro Gly Pro Val Gly						
		530		535		540
Gly Pro Gly Ser Ser Gly Ala Lys Gly Glu Ser Gly Asp Pro Gly Pro						
		545		550		555
Gln Gly Pro Arg Gly Val Gln Gly Pro Pro Gly Pro Thr Gly Lys Pro						
		565		570		575
Gly Lys Arg Gly Arg Pro Gly Ala Asp Gly Gly Arg Gly Met Pro Gly						
		580		585		590
Glu Pro Gly Ala Lys Gly Asp Arg Gly Phe Asp Gly Leu Pro Gly Leu						
		595		600		605
Pro Gly Asp Lys Gly His Arg Gly Glu Arg Gly Pro Gln Gly Pro Pro						
		610		615		620
Gly Pro Pro Gly Asp Asp Gly Met Arg Gly Glu Asp Gly Glu Ile Gly						

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625		630		635		640
Pro Arg Gly Leu	Pro Gly Glu Ala Gly	Pro Arg Gly Leu Leu Gly	Pro			
	645		650		655	
Arg Gly Thr	Pro Gly Ala Pro Gly	Gln Pro Gly Met Ala Gly	Val Asp			
	660	665	670			
Gly Pro Pro Gly	Pro Lys Gly Asn Met Gly	Pro Gln Gly Glu Pro Gly				
	675	680	685			
Pro Pro Gly Gln Gln Gly	Asn Pro Gly Pro Gln Gly	Leu Pro Gly Pro				
	690	695	700			
Gln Gly Pro Ile Gly	Pro Pro Gly Glu Lys Gly	Pro Gln Gly Lys Pro				
	705	710	715			720
Gly Leu Ala Gly Leu	Pro Gly Ala Asp Gly	Pro Pro Gly His Pro Gly				
	725	730	735			
Lys Glu Gly Gln Ser Gly	Glu Lys Gly Ala Leu Gly	Pro Pro Gly Pro				
	740	745	750			
Gln Gly Pro Ile Gly	Xaa Pro Gly Pro Arg Gly	Val Lys Gly Ala Asp				
	755	760	765			
Gly Val Arg Gly Leu	Lys Gly Ser Lys Gly Glu Lys	Gly Glu Asp Gly				
	770	775	780			
Phe Pro Gly Phe Lys	Gly Asp Met Gly Leu Lys	Gly Asp Arg Gly Glu				
	785	790	795			800
Val Gly Gln Ile Gly	Pro Arg Gly Xaa Asp Gly	Pro Glu Gly Pro Lys				
	805	810	815			
Gly Arg Ala Gly	Pro Thr Gly Asp Pro Gly	Pro Ser Gly Gln Ala Gly				
	820	825	830			
Glu Lys Gly Lys Leu	Gly Val Pro Gly Leu Pro Gly	Tyr Pro Gly Arg				
	835	840	845			
Gln Gly Pro Lys Gly	Ser Thr Gly Phe Pro Gly	Phe Pro Gly Ala Asn				
	850	855	860			
Gly Glu Lys Gly Ala	Arg Gly Val Ala Gly Lys	Pro Gly Pro Arg Gly				
	865	870	875			880
Gln Arg Gly Pro Thr	Gly Pro Arg Gly Ser Arg	Gly Ala Arg Gly Pro				
	885	890	895			
Thr Gly Lys Pro Gly	Pro Lys Gly Thr Ser Gly	Gly Asp Gly Pro Pro				
	900	905	910			
Gly Pro Pro Gly Glu	Arg Gly Pro Gln Gly	Pro Gln Gly Pro Val Gly				
	915	920	925			
Phe Pro Gly Pro Lys	Gly Pro Pro Gly Pro Pro	Gly Arg Met Gly Cys				
	930	935	940			
Pro Gly His Pro Gly	Gln Arg Gly Glu Thr Gly	Phe Gln Gly Lys Thr				

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945		950		955		960
Gly Pro Pro Gly	Pro Gly Gly Val Val	Gly Pro Gln Gly	Pro Thr Gly			
	965	970	975			
Glu Thr Gly	Pro Ile Gly Glu Arg Gly Tyr	Pro Gly Pro	Pro Gly Pro			
	980	985	990			
Pro Gly Glu Gln Gly Leu	Pro Gly Ala Ala Gly Lys Glu	Gly Ala Lys				
	995	1000	1005			
Gly Asp Pro Gly Pro Gln Gly	Ile Ser Gly Lys Asp Gly Pro Ala					
	1010	1015	1020			
Gly Leu Arg Gly Phe Pro Gly	Glu Arg Gly Leu Pro Gly Ala Gln					
	1025	1030	1035			
Gly Ala Pro Gly Leu Lys Gly	Gly Glu Gly Pro Gln Gly Pro Pro					
	1040	1045	1050			
Gly Pro Val Gly Ser Pro Gly	Glu Arg Gly Ser Ala Gly Thr Ala					
	1055	1060	1065			
Gly Pro Ile Gly Leu Arg Gly	Arg Pro Gly Pro Gln Gly Pro Pro					
	1070	1075	1080			
Gly Pro Ala Gly Glu Lys Gly	Ala Pro Gly Glu Lys Gly Pro Gln					
	1085	1090	1095			
Gly Pro Ala Gly Arg Asp Gly	Val Gln Gly Pro Val Gly Leu Pro					
	1100	1105	1110			
Gly Pro Ala Gly Pro Ala Gly	Ser Pro Gly Glu Asp Gly Asp Lys					
	1115	1120	1125			
Gly Glu Ile Gly Glu Pro Gly	Gln Lys Gly Ser Lys Gly Gly Lys					
	1130	1135	1140			
Gly Glu Asn Gly Pro Pro Gly	Pro Pro Gly Leu Gln Gly Pro Val					
	1145	1150	1155			
Gly Ala Pro Gly Ile Ala Gly	Gly Asp Gly Glu Pro Gly Pro Arg					
	1160	1165	1170			
Gly Gln Gln Gly Met Phe Gly	Gln Lys Gly Asp Glu Gly Ala Arg					
	1175	1180	1185			
Gly Phe Pro Gly Pro Pro Gly	Pro Ile Gly Leu Gln Gly Leu Pro					
	1190	1195	1200			
Gly Pro Pro Gly Glu Lys Gly	Glu Asn Gly Asp Val Gly Pro Trp					
	1205	1210	1215			
Gly Pro Pro Gly Pro Pro Gly	Pro Arg Gly Pro Gln Gly Pro Asn					
	1220	1225	1230			
Gly Ala Asp Gly Pro Gln Gly	Pro Pro Gly Ser Val Gly Ser Val					
	1235	1240	1245			
Gly Gly Val Gly Glu Lys Gly	Glu Pro Gly Glu Ala Gly Asn Pro					

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1250		1255		1260
Gly Pro Pro Gly Glu Ala	Gly Val Gly Gly Pro	Lys Gly Glu Arg		
1265	1270	1275		
Gly Glu Lys Gly Glu Ala	Gly Pro Pro Gly Ala	Ala Gly Pro Pro		
1280	1285	1290		
Gly Ala Lys Gly Pro Pro	Gly Asp Asp Gly Pro	Lys Gly Asn Pro		
1295	1300	1305		
Gly Pro Val Gly Phe Pro	Gly Asp Pro Gly Pro	Pro Gly Glu Leu		
1310	1315	1320		
Gly Pro Ala Gly Gln Asp	Gly Val Gly Gly Asp	Lys Gly Glu Asp		
1325	1330	1335		
Gly Asp Pro Gly Gln Pro	Gly Pro Pro Gly Pro	Ser Gly Glu Ala		
1340	1345	1350		
Gly Pro Pro Gly Pro Pro	Gly Lys Arg Gly Pro	Pro Gly Ala Ala		
1355	1360	1365		
Gly Ala Glu Gly Arg Gln	Gly Glu Lys Gly Ala	Lys Gly Glu Ala		
1370	1375	1380		
Gly Ala Glu Gly Pro Pro	Gly Lys Thr Gly Pro	Val Gly Pro Gln		
1385	1390	1395		
Gly Pro Ala Gly Lys Pro	Gly Pro Glu Gly Leu	Arg Gly Ile Pro		
1400	1405	1410		
Gly Pro Val Gly Glu Gln	Gly Leu Pro Gly Ala	Ala Gly Gln Asp		
1415	1420	1425		
Gly Pro Pro Gly Pro Met	Gly Pro Pro Gly Leu	Pro Gly Leu Lys		
1430	1435	1440		
Gly Asp Pro Gly Ser Lys	Gly Glu Lys Gly His	Pro Gly Leu Ile		
1445	1450	1455		
Gly Leu Ile Gly Pro Pro	Gly Glu Gln Gly Glu	Lys Gly Asp Arg		
1460	1465	1470		
Gly Leu Pro Gly Thr Gln	Gly Ser Pro Gly Ala	Lys Gly Asp Gly		
1475	1480	1485		
Gly Ile Pro Gly Pro Ala	Gly Pro Leu Gly Pro	Pro Gly Pro Pro		
1490	1495	1500		
Gly Leu Pro Gly Pro Gln	Gly Pro Lys Gly Asn	Lys Gly Ser Thr		
1505	1510	1515		
Gly Pro Ala Gly Gln Lys	Gly Asp Ser Gly Leu	Pro Gly Pro Pro		
1520	1525	1530		
Gly Pro Pro Gly Pro Pro	Gly Glu Val Ile Gln	Pro Leu Pro Ile		
1535	1540	1545		
Leu Ser Ser Lys Lys Thr	Arg Arg His Thr Glu	Gly Met Gln Ala		

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1550		1555		1560
Asp Ala	Asp Asp Asn Ile	Leu Asp Tyr Ser Asp	Gly Met Glu Glu	
1565		1570	1575	
Ile Phe	Gly Ser Leu Asn	Ser Leu Lys Gln Asp	Ile Glu His Met	
1580		1585	1590	
Lys Phe	Pro Met Gly Thr	Gln Thr Asn Pro Ala	Arg Thr Cys Lys	
1595		1600	1605	
Asp Leu	Gln Leu Ser His	Pro Asp Phe Pro Asp	Gly Glu Tyr Trp	
1610		1615	1620	
Ile Asp	Pro Asn Gln Gly	Cys Ser Gly Asp Ser	Phe Lys Val Tyr	
1625		1630	1635	
Cys Asn	Phe Thr Ser Gly	Gly Glu Thr Cys Ile	Tyr Pro Asp Lys	
1640		1645	1650	
Lys Ser	Glu Gly Val Arg	Ile Ser Ser Trp Pro	Lys Glu Lys Pro	
1655		1660	1665	
Gly Ser	Trp Phe Ser Glu	Phe Lys Arg Gly Lys	Leu Leu Ser Tyr	
1670		1675	1680	
Leu Asp	Val Glu Gly Asn	Ser Ile Asn Met Val	Gln Met Thr Phe	
1685		1690	1695	
Leu Lys	Leu Leu Thr Ala	Ser Ala Arg Gln Asn	Phe Thr Tyr His	
1700		1705	1710	
Cys His	Gln Ser Ala Ala	Trp Tyr Asp Val Ser	Ser Gly Ser Tyr	
1715		1720	1725	
Asp Lys	Ala Leu Arg Phe	Leu Gly Ser Asn Asp	Glu Glu Met Ser	
1730		1735	1740	
Tyr Asp	Asn Asn Pro Phe	Ile Lys Thr Leu Tyr	Asp Gly Cys Thr	
1745		1750	1755	
Ser Arg	Lys Gly Tyr Glu	Lys Thr Val Ile Glu	Ile Asn Thr Pro	
1760		1765	1770	
Lys Ile	Asp Gln Val Pro	Ile Val Asp Val Met	Ile Ser Asp Phe	
1775		1780	1785	
Gly Asp	Gln Asn Gln Lys	Phe Gly Phe Glu Val	Gly Pro Val Cys	
1790		1795	1800	
Phe Leu	Gly			
1805				

<210> 57
 <211> 755
 <212> PRT
 <213> Homo sapiens

<400> 57

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Cys Lys Ala Ala Lys Ala Asp Leu Val Phe Met Val Asp Gly Ser Trp
 1 5 10 15
 Ser Ile Gly Asp Glu Asn Phe Asn Lys Ile Ile Ser Phe Leu Tyr Ser
 20 25 30
 Thr Val Gly Ala Leu Asn Lys Ile Gly Thr Asp Gly Thr Gln Val Ala
 35 40 45
 Met Val Gln Phe Thr Asp Asp Pro Arg Thr Glu Phe Lys Leu Asn Ala
 50 55 60
 Tyr Lys Thr Lys Glu Thr Leu Leu Asp Ala Ile Lys His Ile Ser Tyr
 65 70 75 80
 Lys Gly Gly Asn Thr Lys Thr Gly Lys Ala Ile Lys Tyr Val Arg Asp
 85 90 95
 Thr Leu Phe Thr Ala Glu Ser Gly Thr Arg Arg Gly Ile Pro Lys Val
 100 105 110
 Ile Val Val Ile Thr Asp Gly Arg Ser Gln Asp Asp Val Asn Lys Ile
 115 120 125
 Ser Arg Glu Met Gln Leu Asp Gly Tyr Ser Ile Phe Ala Ile Gly Val
 130 135 140
 Ala Asp Ala Asp Tyr Ser Glu Leu Val Ser Ile Gly Ser Lys Pro Ser
 145 150 155 160
 Ala Arg His Val Phe Phe Val Asp Asp Phe Asp Ala Phe Lys Lys Ile
 165 170 175
 Glu Asp Glu Leu Ile Thr Phe Val Cys Glu Thr Ala Ser Ala Thr Cys
 180 185 190
 Pro Val Val His Lys Asp Gly Ile Asp Leu Ala Gly Phe Lys Met Met
 195 200 205
 Glu Met Phe Gly Leu Val Glu Lys Asp Phe Ser Ser Val Glu Gly Val
 210 215 220
 Ser Met Glu Pro Gly Thr Phe Asn Val Phe Pro Cys Tyr Gln Leu His
 225 230 235 240
 Lys Asp Ala Leu Val Ser Gln Pro Thr Arg Tyr Leu His Pro Glu Gly
 245 250 255
 Leu Pro Ser Asp Tyr Thr Ile Ser Phe Leu Phe Arg Ile Leu Pro Asp
 260 265 270
 Thr Pro Gln Glu Pro Phe Ala Leu Trp Glu Ile Leu Asn Lys Asn Ser
 275 280 285
 Asp Pro Leu Val Gly Val Ile Leu Asp Asn Gly Gly Lys Thr Leu Thr
 290 295 300
 Tyr Phe Asn Tyr Asp Gln Ser Gly Asp Phe Gln Thr Val Thr Phe Glu
 305 310 315 320

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Gly Pro Glu Ile Arg Lys Ile Phe Tyr Gly Ser Phe His Lys Leu His
 325 330 335
 Ile Val Val Ser Glu Thr Leu Val Lys Val Val Ile Asp Cys Lys Gln
 340 345 350
 Val Gly Glu Lys Ala Met Asn Ala Ser Ala Asn Ile Thr Ser Asp Gly
 355 360 365
 Val Glu Val Leu Gly Lys Met Val Arg Ser Arg Gly Pro Gly Gly Asn
 370 375 380
 Ser Ala Pro Phe Gln Leu Gln Met Phe Asp Ile Val Cys Ser Thr Ser
 385 390 395 400
 Trp Ala Asn Thr Asp Lys Cys Cys Glu Leu Pro Gly Leu Arg Asp Asp
 405 410 415
 Glu Ser Cys Pro Asp Leu Pro His Ser Cys Ser Cys Ser Glu Thr Asn
 420 425 430
 Glu Val Ala Leu Gly Pro Ala Gly Pro Pro Gly Gly Pro Gly Leu Arg
 435 440 445
 Gly Pro Lys Gly Gln Gln Gly Glu Pro Gly Pro Lys Gly Pro Asp Gly
 450 455 460
 Pro Arg Gly Glu Ile Gly Leu Pro Gly Pro Gln Gly Pro Pro Gly Pro
 465 470 475 480
 Gln Gly Pro Ser Gly Leu Ser Ile Gln Gly Met Pro Gly Met Pro Gly
 485 490 495
 Glu Lys Gly Glu Lys Gly Asp Thr Gly Leu Pro Gly Pro Gln Gly Ile
 500 505 510
 Pro Gly Gly Val Gly Ser Pro Gly Arg Asp Gly Ser Pro Gly Gln Arg
 515 520 525
 Gly Leu Pro Gly Lys Asp Gly Ser Ser Gly Pro Pro Gly Pro Pro Gly
 530 535 540
 Pro Ile Gly Ile Pro Gly Thr Pro Gly Val Pro Gly Ile Thr Gly Ser
 545 550 555 560
 Met Gly Pro Gln Gly Ala Leu Gly Pro Pro Gly Val Pro Gly Ala Lys
 565 570 575
 Gly Glu Arg Gly Glu Arg Gly Asp Leu Gln Ser Gln Ala Met Val Arg
 580 585 590
 Ser Val Ala Arg Gln Val Cys Glu Gln Leu Ile Gln Ser His Met Ala
 595 600 605
 Arg Tyr Thr Ala Ile Leu Asn Gln Ile Pro Ser His Ser Ser Ser Ile
 610 615 620
 Arg Thr Val Gln Gly Pro Pro Gly Glu Pro Gly Arg Pro Gly Ser Pro
 625 630 635 640

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Gly Ala Pro Gly Glu Gln Gly Pro Pro Gly Thr Pro Gly Phe Pro Gly
 645 650 655
 Asn Ala Gly Val Pro Gly Thr Pro Gly Glu Arg Gly Leu Thr Gly Ile
 660 665 670
 Lys Gly Glu Lys Gly Asn Pro Gly Val Gly Thr Gln Gly Pro Arg Gly
 675 680 685
 Pro Pro Gly Pro Ala Gly Pro Ser Gly Glu Ser Arg Pro Gly Ser Pro
 690 695 700
 Gly Pro Pro Gly Ser Pro Gly Pro Arg Gly Pro Pro Gly His Leu Gly
 705 710 715 720
 Val Pro Gly Pro Gln Gly Pro Ser Gly Gln Pro Gly Tyr Cys Asp Pro
 725 730 735
 Ser Ser Cys Ser Ala Tyr Gly Val Arg Asp Leu Ile Pro Tyr Asn Asp
 740 745 750
 Tyr Gln His
 755

<210> 58
 <211> 543
 <212> PRT
 <213> Homo sapiens

<400> 58

Met Gly Thr Ser Leu Ser Pro Asn Asp Pro Trp Pro Leu Asn Pro Leu
 1 5 10 15
 Ser Ile Gln Gln Thr Thr Leu Leu Leu Leu Ser Val Leu Ala Thr
 20 25 30
 Val His Val Gly Gln Arg Leu Leu Arg Gln Arg Arg Arg Gln Leu Arg
 35 40 45
 Ser Ala Pro Pro Gly Pro Phe Ala Trp Pro Leu Ile Gly Asn Ala Ala
 50 55 60
 Ala Val Gly Gln Ala Ala His Leu Ser Phe Ala Arg Leu Ala Arg Arg
 65 70 75 80
 Tyr Gly Asp Val Phe Gln Ile Arg Leu Gly Ser Cys Pro Ile Val Val
 85 90 95
 Leu Asn Gly Glu Arg Ala Ile His Gln Ala Leu Val Gln Gln Gly Ser
 100 105 110
 Ala Phe Ala Asp Arg Pro Ala Phe Ala Ser Phe Arg Val Val Ser Gly
 115 120 125
 Gly Arg Ser Met Ala Phe Gly His Tyr Ser Glu His Trp Lys Val Gln
 130 135 140
 Arg Arg Ala Ala His Ser Met Met Arg Asn Phe Phe Thr Arg Gln Pro
 145 150 155 160

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Arg Ser Arg Gln Val Leu Glu Gly His Val Leu Ser Glu Ala Arg Glu
 165 170 175
 Leu Val Ala Leu Leu Val Arg Gly Ser Ala Asp Gly Ala Phe Leu Asp
 180 185 190
 Pro Arg Pro Leu Thr Val Val Ala Val Ala Asn Val Met Ser Ala Val
 195 200 205
 Cys Phe Gly Cys Arg Tyr Ser His Asp Asp Pro Glu Phe Arg Glu Leu
 210 215 220
 Leu Ser His Asn Glu Glu Phe Gly Arg Thr Val Gly Ala Gly Ser Leu
 225 230 235 240
 Val Asp Val Met Pro Trp Leu Gln Tyr Phe Pro Asn Pro Val Arg Thr
 245 250 255
 Val Phe Arg Glu Phe Glu Gln Leu Asn Arg Asn Phe Ser Asn Phe Ile
 260 265 270
 Leu Asp Lys Phe Leu Arg His Cys Glu Ser Leu Arg Pro Gly Ala Ala
 275 280 285
 Pro Arg Asp Met Met Asp Ala Phe Ile Leu Ser Ala Glu Lys Lys Ala
 290 295 300
 Ala Gly Asp Ser His Gly Gly Gly Ala Arg Leu Asp Leu Glu Asn Val
 305 310 315 320
 Pro Ala Thr Ile Thr Asp Ile Phe Gly Ala Ser Gln Asp Thr Leu Ser
 325 330 335
 Thr Ala Leu Gln Trp Leu Leu Leu Leu Phe Thr Arg Tyr Pro Asp Val
 340 345 350
 Gln Thr Arg Val Gln Ala Glu Leu Asp Gln Val Val Gly Arg Asp Arg
 355 360 365
 Leu Pro Cys Met Gly Asp Gln Pro Asn Leu Pro Tyr Val Leu Ala Phe
 370 375 380
 Leu Tyr Glu Ala Met Arg Phe Ser Ser Phe Val Pro Val Thr Ile Pro
 385 390 395 400
 His Ala Thr Thr Ala Asn Thr Ser Val Leu Gly Tyr His Ile Pro Lys
 405 410 415
 Asp Thr Val Val Phe Val Asn Gln Trp Ser Val Asn His Asp Pro Val
 420 425 430
 Lys Trp Pro Asn Pro Glu Asn Phe Asp Pro Ala Arg Phe Leu Asp Lys
 435 440 445
 Asp Gly Leu Ile Asn Lys Asp Leu Thr Ser Arg Val Met Ile Phe Ser
 450 455 460
 Val Gly Lys Arg Arg Cys Ile Gly Glu Glu Leu Ser Lys Met Gln Leu
 465 470 475 480

Phe	Leu	Phe	Ile	Ser	Ile	Leu	Ala	His	Gln	Cys	Asp	Phe	Arg	Ala	Asn	
				485					490					495		
Pro	Asn	Glu	Pro	Ala	Lys	Met	Asn	Phe	Ser	Tyr	Gly	Leu	Thr	Ile	Lys	
				500					505					510		
Pro	Lys	Ser	Phe	Lys	Val	Asn	Val	Thr	Leu	Arg	Glu	Ser	Met	Glu	Leu	
				515					520					525		
Leu	Asp	Ser	Ala	Val	Gln	Asn	Leu	Gln	Ala	Lys	Glu	Thr	Cys	Gln		
				530					535					540		

<400> 59

Met 1	Ser	Gln	Arg	Pro 5	Arg	Ala	Pro	Arg	Ser 10	Ala	Leu	Trp	Leu	Leu 15	Ala
Pro	Pro	Leu	Leu 20	Arg	Trp	Ala	Pro	Pro 25	Leu	Leu	Thr	Val	Leu 30	His	Ser
Asp	Leu	Phe 35	Gln	Ala	Leu	Leu	Asp 40	Ile	Leu	Asp	Tyr	Tyr 45	Glu	Ala	Ser
Leu	Ser 50	Glu	Ser	Gln	Lys	Tyr 55	Arg	Tyr	Gln	Asp	Glu 60	Asp	Thr	Pro	Pro
Leu 65	Glu	His	Ser	Pro	Ala 70	His	Leu	Pro	Asn	Gln 75	Ala	Asn	Ser	Pro	Pro 80
Val	Ile	Val	Asn 85	Thr	Asp	Thr	Leu	Glu	Ala 90	Pro	Gly	Tyr	Glu 95	Leu	Gln
Val	Asn	Gly	Thr 100	Glu	Gly	Glu	Met	Glu 105	Tyr	Glu	Glu	Ile	Thr 110	Leu	Glu
Arg	Gly	Asn 115	Ser	Gly	Leu	Gly	Phe 120	Ser	Ile	Ala	Gly	Gly 125	Thr	Asp	Asn
Pro	His 130	Ile	Gly	Asp	Asp	Pro 135	Ser	Ile	Phe	Ile	Thr 140	Lys	Ile	Ile	Pro
Gly 145	Gly	Ala	Ala	Ala	Gln 150	Asp	Gly	Arg	Leu	Arg 155	Val	Asn	Asp	Ser	Ile 160
Leu	Phe	Val	Asn 165	Glu	Val	Asp	Val	Arg	Glu 170	Val	Thr	His	Ser	Ala 175	Ala
Val	Glu	Ala	Leu 180	Lys	Glu	Ala	Gly	Ser 185	Ile	Val	Arg	Leu	Tyr 190	Val	Met
Arg	Arg	Lys 195	Pro	Pro	Ala	Glu	Lys 200	Val	Met	Glu	Ile	Lys 205	Leu	Ile	Lys
Gly	Pro	Lys	Gly	Leu	Gly	Phe	Ser	Ile	Ala	Gly	Gly	Val	Gly	Asn	Gln

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210	215	220
His Ile Pro Gly Asp	Asn Ser Ile Tyr Val	Thr Lys Ile Ile Glu Gly
225	230	235 240
Gly Ala Ala His Lys Asp Gly Arg Leu Gln	Ile Gly Asp Lys Ile Leu	
	245	250 255
Ala Val Asn Ser Val Gly Leu Glu Asp Val Met His Glu Asp Ala Val		
	260	265 270
Ala Ala Leu Lys Asn Thr Tyr Asp Val Val Tyr Leu Lys Val Ala Lys		
	275	280 285
Pro Ser Asn Ala Tyr Leu Ser Asp Ser Tyr Ala Pro Pro Asp Ile Thr		
	290	295 300
Thr Ser Tyr Ser Gln His Leu Asp Asn Glu Ile Ser His Ser Ser Tyr		
	305	310 315 320
Leu Gly Thr Asp Tyr Pro Thr Ala Met Thr Pro Thr Ser Pro Arg Arg		
	325	330 335
Tyr Ser Pro Val Ala Lys Asp Leu Leu Gly Glu Glu Asp Ile Pro Arg		
	340	345 350
Glu Pro Arg Arg Ile Val Ile His Arg Gly Ser Thr Gly Leu Gly Phe		
	355	360 365
Asn Ile Val Gly Gly Glu Asp Gly Glu Gly Ile Phe Ile Ser Phe Ile		
	370	375 380
Leu Ala Gly Gly Pro Ala Asp Leu Ser Gly Glu Leu Arg Lys Gly Asp		
	385	390 395 400
Gln Ile Leu Ser Val Asn Gly Val Asp Leu Arg Asn Ala Ser His Glu		
	405	410 415
Gln Ala Ala Ile Ala Leu Lys Asn Ala Gly Gln Thr Val Thr Ile Ile		
	420	425 430
Ala Gln Tyr Lys Pro Glu Glu Tyr Ser Arg Phe Glu Ala Lys Ile His		
	435	440 445
Asp Leu Arg Glu Gln Leu Met Asn Ser Ser Leu Gly Ser Gly Thr Ala		
	450	455 460
Ser Leu Arg Ser Asn Pro Lys Arg Gly Phe Tyr Ile Arg Ala Leu Phe		
	465	470 475 480
Asp Tyr Asp Lys Thr Lys Asp Cys Gly Phe Leu Ser Gln Ala Leu Ser		
	485	490 495
Phe Arg Phe Gly Asp Val Leu His Val Ile Asp Ala Ser Asp Glu Glu		
	500	505 510
Trp Trp Gln Ala Arg Arg Val His Ser Asp Ser Glu Thr Asp Asp Ile		
	515	520 525
Gly Phe Ile Pro Ser Lys Arg Arg Val Glu Arg Arg Glu Trp Ser Arg		

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530 535 540
 Leu Lys Ala Lys Asp Trp Gly Ser Ser Ser Gly Ser Gln Gly Arg Glu
 545 550 555 560
 Asp Ser Val Leu Ser Tyr Glu Thr Val Thr Gln Met Glu Val His Tyr
 565 570 575
 Ala Arg Pro Ile Ile Ile Leu Gly Pro Thr Lys Asp Arg Ala Asn Asp
 580 585 590
 Asp Leu Leu Ser Glu Phe Pro Asp Lys Phe Gly Ser Cys Val Pro His
 595 600 605
 Thr Thr Arg Pro Lys Arg Glu Tyr Glu Ile Asp Gly Arg Asp Tyr His
 610 615 620
 Phe Val Ser Ser Arg Glu Lys Met Glu Lys Asp Ile Gln Ala His Lys
 625 630 635 640
 Phe Ile Glu Ala Gly Gln Tyr Asn Ser His Leu Tyr Gly Thr Ser Val
 645 650 655
 Gln Ser Val Arg Glu Val Ala Glu Gln Gly Lys His Cys Ile Leu Asp
 660 665 670
 Val Ser Ala Asn Ala Val Arg Arg Leu Gln Ala Ala His Leu His Pro
 675 680 685
 Ile Ala Ile Phe Ile Arg Pro Arg Ser Leu Glu Asn Val Leu Glu Ile
 690 695 700
 Asn Lys Arg Ile Thr Glu Glu Gln Ala Arg Lys Ala Phe Asp Arg Ala
 705 710 715 720
 Thr Lys Leu Glu Gln Glu Phe Thr Glu Cys Phe Ser Ala Ile Val Glu
 725 730 735
 Gly Asp Ser Phe Glu Glu Ile Tyr His Lys Val Lys Arg Val Ile Glu
 740 745 750
 Asp Leu Ser Gly Pro Tyr Ile Trp Val Pro Ala Arg Glu Arg Leu
 755 760 765

 <210> 60
 <211> 367
 <212> PRT
 <213> Homo sapiens

 <400> 60

 Met Val Met Glu Val Gly Thr Leu Asp Ala Gly Gly Leu Arg Ala Leu
 1 5 10 15
 Leu Gly Glu Arg Ala Ala Gln Cys Leu Leu Leu Asp Cys Arg Ser Phe
 20 25 30
 Phe Ala Phe Asn Ala Gly His Ile Ala Gly Ser Val Asn Val Arg Phe
 35 40 45

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Ser Thr Ile Val Arg Arg Arg Ala Lys Gly Ala Met Gly Leu Glu His
 50 55 60
 Ile Val Pro Asn Ala Glu Leu Arg Gly Arg Leu Leu Ala Gly Ala Tyr
 65 70 75 80
 His Ala Val Val Leu Leu Asp Glu Arg Ser Ala Ala Leu Asp Gly Ala
 85 90 95
 Lys Arg Asp Gly Thr Leu Ala Leu Ala Gly Ala Leu Cys Arg Glu
 100 105 110
 Ala Arg Ala Ala Gln Val Phe Phe Leu Lys Gly Gly Tyr Glu Ala Phe
 115 120 125
 Ser Ala Ser Cys Pro Glu Leu Cys Ser Lys Gln Ser Thr Pro Met Gly
 130 135 140
 Leu Ser Leu Pro Leu Ser Thr Ser Val Pro Asp Ser Ala Glu Ser Gly
 145 150 155 160
 Cys Ser Ser Cys Ser Thr Pro Leu Tyr Asp Gln Gly Gly Pro Val Glu
 165 170 175
 Ile Leu Pro Phe Leu Tyr Leu Gly Ser Ala Tyr His Ala Ser Arg Lys
 180 185 190
 Asp Met Leu Asp Ala Leu Gly Ile Thr Ala Leu Ile Asn Val Ser Ala
 195 200 205
 Asn Cys Pro Asn His Phe Glu Gly His Tyr Gln Tyr Lys Ser Ile Pro
 210 215 220
 Val Glu Asp Asn His Lys Ala Asp Ile Ser Ser Trp Phe Asn Glu Ala
 225 230 235 240
 Ile Asp Phe Ile Asp Ser Ile Lys Asn Ala Gly Gly Arg Val Phe Val
 245 250 255
 His Cys Gln Ala Gly Ile Ser Arg Ser Ala Thr Ile Cys Leu Ala Tyr
 260 265 270
 Leu Met Arg Thr Asn Arg Val Lys Leu Asp Glu Ala Phe Glu Phe Val
 275 280 285
 Lys Gln Arg Arg Ser Ile Ile Ser Pro Asn Phe Ser Phe Met Gly Gln
 290 295 300
 Leu Leu Gln Phe Glu Ser Gln Val Leu Ala Pro His Cys Ser Ala Glu
 305 310 315 320
 Ala Gly Ser Pro Ala Met Ala Val Leu Asp Arg Gly Thr Ser Thr Thr
 325 330 335
 Thr Val Phe Asn Phe Pro Val Ser Ile Pro Val His Ser Thr Asn Ser
 340 345 350
 Ala Leu Ser Tyr Leu Gln Ser Pro Ile Thr Thr Ser Pro Ser Cys
 355 360 365

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<210> 61
 <211> 345
 <212> PRT
 <213> Homo sapiens

<400> 61

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Met Ala Ala Ala Glu Pro Ala Ser Ser Gly Gln Gln Ala Pro Ala Gly
1          5          10          15

Gln Gly Gln Gly Gln Arg Pro Pro Pro Gln Pro Pro Gln Ala Gln Ala
          20          25          30

Pro Gln Pro Pro Pro Pro Pro Gln Leu Gly Gly Ala Gly Gly Gly Ser
          35          40          45

Ser Arg His Glu Lys Ser Leu Gly Leu Leu Thr Thr Lys Phe Val Ser
          50          55          60

Leu Leu Gln Glu Ala Lys Asp Gly Val Leu Asp Leu Lys Ala Ala Ala
65          70          75          80

Asp Thr Leu Ala Val Arg Gln Lys Arg Arg Ile Tyr Asp Ile Thr Asn
          85          90          95

Val Leu Glu Gly Ile Asp Leu Ile Glu Lys Lys Ser Lys Asn Ser Ile
          100          105          110

Gln Trp Lys Gly Val Gly Ala Gly Cys Asn Thr Lys Glu Val Ile Asp
          115          120          125

Arg Leu Arg Tyr Leu Lys Ala Glu Ile Glu Asp Leu Glu Leu Lys Glu
          130          135          140

Arg Glu Leu Asp Gln Gln Lys Leu Trp Leu Gln Gln Ser Ile Lys Asn
145          150          155          160

Val Met Asp Asp Ser Ile Asn Asn Arg Phe Ser Tyr Val Thr His Glu
          165          170          175

Asp Ile Cys Asn Cys Phe Asn Gly Asp Thr Leu Leu Ala Ile Gln Ala
          180          185          190

Pro Ser Gly Thr Gln Leu Glu Val Pro Ile Pro Glu Met Gly Gln Asn
          195          200          205

Gly Gln Lys Lys Tyr Gln Ile Asn Leu Lys Ser His Ser Gly Pro Ile
          210          215          220

His Val Leu Leu Ile Asn Lys Glu Ser Ser Ser Ser Lys Pro Val Val
225          230          235          240

Phe Pro Val Pro Pro Pro Asp Asp Leu Thr Gln Pro Ser Ser Gln Ser
          245          250          255

Leu Thr Pro Val Thr Pro Gln Lys Ser Ser Met Ala Thr Gln Asn Leu
          260          265          270

Pro Glu Gln His Val Ser Glu Arg Ser Gln Ala Leu Gln Gln Thr Ser
          275          280          285

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Ala Thr Asp Ile Ser Ser Gly Ser Ile Ser Gly Asp Ile Ile Asp Glu
 290 295 300

Leu Met Ser Ser Asp Val Phe Pro Leu Leu Arg Leu Ser Pro Thr Pro
 305 310 315 320

Ala Asp Asp Tyr Asn Phe Asn Leu Asp Asp Asn Glu Gly Val Cys Asp
 325 330 335

Leu Phe Asp Val Gln Ile Leu Asn Tyr
 340 345

<210> 62

<211> 427

<212> PRT

<213> Homo sapiens

<400> 62

Met Glu Thr Leu Cys Leu Arg Ala Ser Phe Trp Leu Ala Leu Val Gly
 1 5 10 15

Cys Val Ile Ser Asp Asn Pro Glu Arg Tyr Ser Thr Asn Leu Ser Asn
 20 25 30

His Val Asp Asp Phe Thr Thr Phe Arg Gly Thr Glu Leu Ser Phe Leu
 35 40 45

Val Thr Thr His Gln Pro Thr Asn Leu Val Leu Pro Ser Asn Gly Ser
 50 55 60

Met His Asn Tyr Cys Pro Gln Gln Thr Lys Ile Thr Ser Ala Phe Lys
 65 70 75 80

Tyr Ile Asn Thr Val Ile Ser Cys Thr Ile Phe Ile Val Gly Met Val
 85 90 95

Gly Asn Ala Thr Leu Leu Arg Ile Ile Tyr Gln Asn Lys Cys Met Arg
 100 105 110

Asn Gly Pro Asn Ala Leu Ile Ala Ser Leu Ala Leu Gly Asp Leu Ile
 115 120 125

Tyr Val Val Ile Asp Leu Pro Ile Asn Val Phe Lys Leu Leu Ala Gly
 130 135 140

Arg Trp Pro Phe Asp His Asn Asp Phe Gly Val Phe Leu Cys Lys Leu
 145 150 155 160

Phe Pro Phe Leu Gln Lys Ser Ser Val Gly Ile Thr Val Leu Asn Leu
 165 170 175

Cys Ala Leu Ser Val Asp Arg Tyr Arg Ala Val Ala Ser Trp Ser Arg
 180 185 190

Val Gln Gly Ile Gly Ile Pro Leu Val Thr Ala Ile Glu Ile Val Ser
 195 200 205

Ile Trp Ile Leu Ser Phe Ile Leu Ala Ile Pro Glu Ala Ile Gly Phe

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210	215	220
Val Met Val Pro Phe Glu Tyr Arg Gly Glu Gln His Lys Thr Cys Met		
225	230	235 240
Leu Asn Ala Thr Ser Lys Phe Met Glu Phe Tyr Gln Asp Val Lys Asp		
	245	250 255
Trp Trp Leu Phe Gly Phe Tyr Phe Cys Met Pro Leu Val Cys Thr Ala		
	260	265 270
Ile Phe Tyr Thr Leu Met Thr Cys Glu Met Leu Asn Arg Arg Asn Gly		
	275	280 285
Ser Leu Arg Ile Ala Leu Ser Glu His Leu Lys Gln Arg Arg Glu Val		
	290	295 300
Ala Lys Thr Val Phe Cys Leu Val Val Ile Phe Ala Leu Cys Trp Phe		
	305	310 315 320
Pro Leu His Leu Ser Arg Ile Leu Lys Lys Thr Val Tyr Asn Glu Met		
	325	330 335
Asp Lys Asn Arg Cys Glu Leu Leu Ser Phe Leu Leu Leu Met Asp Tyr		
	340	345 350
Ile Gly Ile Asn Leu Ala Thr Met Asn Ser Cys Ile Asn Pro Ile Ala		
	355	360 365
Leu Tyr Phe Val Ser Lys Lys Phe Lys Asn Cys Phe Gln Ser Cys Leu		
	370	375 380
Cys Cys Cys Cys Tyr Gln Ser Lys Ser Leu Met Thr Ser Val Pro Met		
	385	390 395 400
Asn Gly Thr Ser Ile Gln Trp Lys Asn His Asp Gln Asn Asn His Asn		
	405	410 415
Thr Asp Arg Ser Ser His Lys Asp Ser Met Asn		
	420	425

<210> 63
 <211> 405
 <212> PRT
 <213> Homo sapiens
 <400> 63

Met Glu Arg Leu Gln Lys Gln Pro Leu Thr Ser Pro Gly Ser Val Ser
1 5 10 15
Pro Ser Arg Asp Ser Ser Val Pro Gly Ser Pro Ser Ser Ile Val Ala
20 25 30
Lys Met Asp Asn Gln Val Leu Gly Tyr Lys Asp Leu Ala Ala Ile Pro
35 40 45
Lys Asp Lys Ala Ile Leu Asp Ile Glu Arg Pro Asp Leu Met Ile Tyr
50 55 60

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Glu	Pro	His	Phe	Thr	Tyr	Ser	Leu	Leu	Glu	His	Val	Glu	Leu	Pro	Arg	65	70	75	80
Gln	Arg	Glu	Arg	Ser	Leu	Ser	Pro	Lys	Ser	Thr	Ser	Pro	Pro	Pro	Ser	85	90	95	
Pro	Glu	Val	Trp	Ala	Asp	Ser	Arg	Ser	Pro	Gly	Ile	Ile	Ser	Gln	Ala	100	105	110	
Ser	Ala	Pro	Arg	Thr	Thr	Gly	Thr	Pro	Arg	Thr	Ser	Leu	Pro	His	Phe	115	120	125	
His	His	Pro	Glu	Thr	Ser	Arg	Pro	Asp	Ser	Asn	Ile	Tyr	Lys	Lys	Pro	130	135	140	
Pro	Ile	Tyr	Lys	Gln	Arg	Glu	Ser	Val	Gly	Gly	Ser	Pro	Gln	Thr	Lys	145	150	155	160
His	Leu	Ile	Glu	Asp	Leu	Ile	Ile	Glu	Ser	Ser	Lys	Phe	Pro	Ala	Ala	165	170	175	
Gln	Pro	Pro	Asp	Pro	Asn	Gln	Pro	Ala	Lys	Ile	Glu	Thr	Asp	Tyr	Trp	180	185	190	
Pro	Cys	Pro	Pro	Ser	Leu	Ala	Val	Val	Glu	Thr	Glu	Trp	Arg	Lys	Arg	195	200	205	
Lys	Ala	Ser	Arg	Arg	Gly	Ala	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Asp	Asp	210	215	220	
Asp	Ser	Gly	Glu	Glu	Met	Lys	Ala	Leu	Arg	Glu	Arg	Gln	Arg	Glu	Glu	225	230	235	240
Leu	Ser	Lys	Val	Thr	Ser	Asn	Leu	Gly	Lys	Met	Ile	Leu	Lys	Glu	Glu	245	250	255	
Met	Glu	Lys	Ser	Leu	Pro	Ile	Arg	Arg	Lys	Thr	Arg	Ser	Leu	Pro	Asp	260	265	270	
Arg	Thr	Pro	Phe	His	Thr	Ser	Leu	His	Gln	Gly	Thr	Ser	Lys	Ser	Ser	275	280	285	
Ser	Leu	Pro	Arg	Tyr	Gly	Arg	Thr	Thr	Leu	Ser	Arg	Leu	Gln	Ser	Thr	290	295	300	
Glu	Phe	Ser	Pro	Ser	Gly	Ser	Glu	Thr	Gly	Ser	Pro	Gly	Leu	Gln	Asn	305	310	315	320
Gly	Glu	Gly	Gln	Arg	Gly	Arg	Met	Asp	Arg	Gly	Asn	Ser	Leu	Pro	Cys	325	330	335	
Val	Leu	Glu	Gln	Lys	Ile	Tyr	Pro	Tyr	Glu	Met	Leu	Val	Val	Thr	Asn	340	345	350	
Lys	Gly	Arg	Thr	Lys	Leu	Pro	Pro	Gly	Val	Asp	Arg	Met	Arg	Leu	Glu	355	360	365	
Arg	His	Leu	Ser	Ala	Glu	Asp	Phe	Ser	Arg	Val	Phe	Ala	Met	Ser	Pro	370	375	380	

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Glu Glu Phe Gly Lys Leu Ala Leu Trp Lys Arg Asn Glu Leu Lys Lys
 385 390 395 400

Lys Ala Ser Leu Phe
 405

<210> 64

<211> 916

<212> PRT

<213> Homo sapiens

<400> 64

Met Glu Ser Gly Gln Pro Ala Arg Arg Ile Ala Met Ala Pro Leu Leu
 1 5 10 15

Glu Tyr Glu Arg Gln Leu Val Leu Glu Leu Leu Asp Thr Asp Gly Leu
 20 25 30

Val Val Cys Ala Arg Gly Leu Gly Ala Asp Arg Leu Leu Tyr His Phe
 35 40 45

Leu Gln Leu His Cys His Pro Ala Cys Leu Val Leu Val Leu Asn Thr
 50 55 60

Gln Pro Ala Glu Glu Glu Tyr Phe Ile Asn Gln Leu Lys Ile Glu Gly
 65 70 75 80

Val Glu His Leu Pro Arg Arg Val Thr Asn Glu Ile Thr Ser Asn Ser
 85 90 95

Arg Tyr Glu Val Tyr Thr Gln Gly Gly Val Ile Phe Ala Thr Ser Arg
 100 105 110

Ile Leu Val Val Asp Phe Leu Thr Asp Arg Ile Pro Ser Asp Leu Ile
 115 120 125

Thr Gly Ile Leu Val Tyr Arg Ala His Arg Ile Ile Glu Ser Cys Gln
 130 135 140

Glu Ala Phe Ile Leu Arg Leu Phe Arg Gln Lys Asn Lys Arg Gly Phe
 145 150 155 160

Ile Lys Ala Phe Thr Asp Asn Ala Val Ala Phe Asp Thr Gly Phe Cys
 165 170 175

His Val Glu Arg Val Met Arg Asn Leu Phe Val Arg Lys Leu Tyr Leu
 180 185 190

Trp Pro Arg Phe His Val Ala Val Asn Ser Phe Leu Glu Gln His Lys
 195 200 205

Pro Glu Val Val Glu Ile His Val Ser Met Thr Pro Thr Met Leu Ala
 210 215 220

Ile Gln Thr Ala Ile Leu Asp Ile Leu Asn Ala Cys Leu Lys Glu Leu
 225 230 235 240

Lys Cys His Asn Pro Ser Leu Glu Val Glu Asp Leu Ser Leu Glu Asn
 245 250 255

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Ala Ile Gly Lys Pro Phe Asp Lys Thr Ile Arg His Tyr Leu Asp Pro
 260 265 270
 Leu Trp His Gln Leu Gly Ala Lys Thr Lys Ser Leu Val Gln Asp Leu
 275 280 285
 Lys Ile Leu Arg Thr Leu Leu Gln Tyr Leu Ser Gln Tyr Asp Cys Val
 290 295 300
 Thr Phe Leu Asn Leu Leu Glu Ser Leu Arg Ala Thr Glu Lys Ala Phe
 305 310 315 320
 Gly Gln Asn Ser Gly Trp Leu Phe Leu Asp Ser Ser Thr Ser Met Phe
 325 330 335
 Ile Asn Ala Arg Ala Arg Val Tyr His Leu Pro Asp Ala Lys Met Ser
 340 345 350
 Lys Lys Glu Lys Ile Ser Glu Lys Met Glu Ile Lys Glu Gly Glu Glu
 355 360 365
 Thr Lys Lys Glu Leu Val Leu Glu Ser Asn Pro Lys Trp Glu Ala Leu
 370 375 380
 Thr Glu Val Leu Lys Glu Ile Glu Ala Glu Asn Lys Glu Ser Glu Ala
 385 390 395 400
 Leu Gly Gly Pro Gly Gln Val Leu Ile Cys Ala Ser Asp Asp Arg Thr
 405 410 415
 Cys Ser Gln Leu Arg Asp Tyr Ile Thr Leu Gly Ala Glu Ala Phe Leu
 420 425 430
 Leu Arg Leu Tyr Arg Lys Thr Phe Glu Lys Asp Ser Lys Ala Glu Glu
 435 440 445
 Val Trp Met Lys Phe Arg Lys Glu Asp Ser Ser Lys Arg Ile Arg Lys
 450 455 460
 Ser His Lys Arg Pro Lys Asp Pro Gln Asn Lys Glu Arg Ala Ser Thr
 465 470 475 480
 Lys Glu Arg Thr Leu Lys Lys Lys Lys Arg Lys Leu Thr Leu Thr Gln
 485 490 495
 Met Val Gly Lys Pro Glu Glu Leu Glu Glu Glu Gly Asp Val Glu Glu
 500 505 510
 Gly Tyr Arg Arg Glu Ile Ser Ser Ser Pro Glu Ser Cys Pro Glu Glu
 515 520 525
 Ile Lys His Glu Glu Phe Asp Val Asn Leu Ser Ser Asp Ala Ala Phe
 530 535 540
 Gly Ile Leu Lys Glu Pro Leu Thr Ile Ile His Pro Leu Leu Gly Cys
 545 550 555 560
 Ser Asp Pro Tyr Ala Leu Thr Arg Val Leu His Glu Val Glu Pro Arg
 565 570 575

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Tyr Val Val Leu Tyr Asp Ala Glu Leu Thr Phe Val Arg Gln Leu Glu
 580 585 590
 Ile Tyr Arg Ala Ser Arg Pro Gly Lys Pro Leu Arg Val Tyr Phe Leu
 595 600 605
 Ile Tyr Gly Gly Ser Thr Glu Glu Gln Arg Tyr Leu Thr Ala Leu Arg
 610 615 620
 Lys Glu Lys Glu Ala Phe Glu Lys Leu Ile Arg Glu Lys Ala Ser Met
 625 630 635 640
 Val Val Pro Glu Glu Arg Glu Gly Arg Asp Glu Thr Asn Leu Asp Leu
 645 650 655
 Val Arg Gly Thr Ala Ser Ala Asp Val Ser Thr Asp Thr Arg Lys Ala
 660 665 670
 Gly Gly Gln Glu Gln Asn Gly Thr Gln Gln Ser Ile Val Val Asp Met
 675 680 685
 Arg Glu Phe Arg Ser Glu Leu Pro Ser Leu Ile His Arg Arg Gly Ile
 690 695 700
 Asp Ile Glu Pro Val Thr Leu Glu Val Gly Asp Tyr Ile Leu Thr Pro
 705 710 715 720
 Glu Met Cys Val Glu Arg Lys Ser Ile Ser Asp Leu Ile Gly Ser Leu
 725 730 735
 Asn Asn Gly Arg Leu Tyr Ser Gln Cys Ile Ser Met Ser Arg Tyr Tyr
 740 745 750
 Lys Arg Pro Val Leu Leu Ile Glu Phe Asp Pro Ser Lys Pro Phe Ser
 755 760 765
 Leu Thr Ser Arg Gly Ala Leu Phe Gln Glu Ile Ser Ser Asn Asp Ile
 770 775 780
 Ser Ser Lys Leu Thr Leu Leu Thr Leu His Phe Pro Arg Leu Arg Ile
 785 790 795 800
 Leu Trp Cys Pro Ser Pro His Ala Thr Ala Glu Leu Phe Glu Glu Leu
 805 810 815
 Lys Gln Ser Lys Pro Gln Pro Asp Ala Ala Thr Ala Leu Ala Ile Thr
 820 825 830
 Ala Asp Ser Glu Thr Leu Pro Glu Ser Glu Lys Tyr Asn Pro Gly Pro
 835 840 845
 Gln Asp Phe Leu Leu Lys Met Pro Gly Val Asn Ala Lys Asn Cys Arg
 850 855 860
 Ser Leu Met His His Val Lys Asn Ile Ala Glu Leu Ala Ala Leu Ser
 865 870 875 880
 Gln Asp Glu Leu Thr Ser Ile Leu Gly Asn Ala Ala Asn Ala Lys Gln
 885 890 895

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Leu Tyr Asp Phe Ile His Thr Ser Phe Ala Glu Val Val Ser Lys Gly
 900 905 910

Lys Gly Lys Lys
 915

<210> 65
 <211> 297
 <212> PRT
 <213> Homo sapiens

<400> 65

Glu Phe Gly Ala Lys Ser Asn Gln Gln Leu Asp Arg Lys Arg Met Ala
 1 5 10 15

Leu Lys Gln Ile Ser Ser Asn Lys Cys Phe Gly Gly Leu Gln Lys Val
 20 25 30

Phe Glu His Asp Ser Val Glu Leu Asn Cys Lys Met Lys Phe Ala Val
 35 40 45

Tyr Leu Pro Pro Lys Ala Glu Thr Gly Lys Cys Pro Ala Cys Ile Gly
 50 55 60

Ser Pro Gly Leu Thr Cys Thr Glu Pro Lys Phe Tyr His Gln Asn Leu
 65 70 75 80

Val Ile Ile Ser Leu Leu Gln Asn His Leu Ser Cys Cys His Cys Ser
 85 90 95

Arg Tyr Ser Pro Arg Ala Cys Asn Ile Lys Gly Glu Asp Glu Ser Trp
 100 105 110

Asp Phe Ala Thr Gly Arg Gly Phe Tyr Val Asp Ala Thr Glu Asp Pro
 115 120 125

Trp Lys Thr Asn Tyr Arg Met Tyr Ser Tyr Val Thr Glu Glu Leu Pro
 130 135 140

Gln Leu Ile Asn Ala Asn Phe Pro Val Asp Pro Gln Arg Met Ser Ile
 145 150 155 160

Phe Gly His Ser Met Gly Gly His Gly Ala Leu Ile Cys Ala Leu Lys
 165 170 175

Asn Pro Gly Lys Tyr Lys Ser Val Ser Ala Phe Ala Pro Ile Cys Asn
 180 185 190

Pro Val Leu Cys Pro Trp Gly Lys Lys Ala Phe Ser Gly Tyr Leu Gly
 195 200 205

Thr Asp Gln Ser Lys Trp Lys Ala Tyr Asp Ala Thr His Leu Val Lys
 210 215 220

Ser Tyr Pro Gly Ser Gln Leu Asp Ile Leu Ile Asp Gln Gly Lys Asp
 225 230 235 240

Asp Gln Phe Leu Leu Asp Gly Gln Leu Leu Pro Asp Asn Phe Ile Ala

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	245		250		255
Ala Cys Thr	Glu Lys Lys Ile Pro Val Val Phe Arg Leu Gln Glu Gly				
	260		265		270
Tyr Asp His Ser Tyr Tyr Phe Ile Ala Thr Phe Ile Thr Asp His Ile					
	275		280		285
Arg His His Ala Lys Tyr Leu Asn Ala					
	290		295		
<210> 66					
<211> 756					
<212> PRT					
<213> Homo sapiens					
<400> 66					
Met Ser Pro Gln Lys Arg Val Lys Asn Val Gln Ala Gln Asn Arg Thr					
1	5		10		15
Ser Gln Gly Ser Ser Ser Phe Gln Thr Thr Leu Ser Ala Trp Lys Val					
	20		25		30
Lys Gln Asp Pro Ser Asn Ser Lys Asn Ile Ser Lys His Gly Gln Asn					
	35		40		45
Asn Pro Val Gly Asp Tyr Glu His Ala Asp Asp Gln Ala Glu Glu Asp					
	50		55		60
Ala Leu Gln Met Ala Val Gly Tyr Phe Glu Lys Gly Pro Ile Lys Ala					
65	70		75		80
Ser Gln Asn Lys Asp Lys Thr Leu Glu Lys His Leu Lys Thr Val Glu					
	85		90		95
Asn Val Ala Trp Lys Asn Gly Leu Ala Ser Glu Glu Ile Asp Ile Leu					
	100		105		110
Leu Asn Ile Ala Leu Ser Gly Lys Phe Gly Asn Ala Val Asn Thr Arg					
	115		120		125
Ile Leu Lys Cys Met Ile Pro Ala Thr Val Ile Ser Glu Asp Ser Val					
	130		135		140
Val Lys Ala Val Ser Trp Leu Cys Val Gly Lys Cys Ser Gly Ser Thr					
145	150		155		160
Lys Val Leu Phe Tyr Arg Trp Leu Val Ala Met Phe Asp Phe Ile Asp					
	165		170		175
Arg Lys Glu Gln Ile Asn Leu Leu Tyr Gly Phe Phe Phe Ala Ser Leu					
	180		185		190
Gln Asp Asp Ala Leu Cys Pro Tyr Val Cys His Leu Leu Tyr Leu Leu					
	195		200		205
Thr Lys Lys Glu Asn Val Lys Pro Phe Arg Val Arg Lys Leu Leu Asp					
	210		215		220

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Leu	Gln	Ala	Lys	Met	Gly	Met	Gln	Pro	His	Leu	Gln	Ala	Leu	Leu	Ser	
225					230					235					240	
Leu	Tyr	Lys	Phe	Phe	Ala	Pro	Ala	Leu	Ile	Ser	Val	Ser	Leu	Pro	Val	
				245					250					255		
Arg	Lys	Lys	Ile	Tyr	Leu	Gln	Asn	Ser	Glu	Asn	Leu	Trp	Lys	Thr	Ala	
			260					265					270			
Leu	Leu	Ala	Val	Lys	Gln	Arg	Asn	Arg	Gly	Pro	Ser	Pro	Glu	Pro	Leu	
		275					280					285				
Lys	Leu	Met	Leu	Gly	Pro	Ala	Asn	Val	Arg	Pro	Leu	Lys	Arg	Lys	Trp	
	290					295					300					
Asn	Ser	Leu	Ser	Val	Ile	Pro	Val	Leu	Asn	Ser	Ser	Ser	Tyr	Thr	Lys	
305					310					315					320	
Glu	Cys	Gly	Lys	Lys	Glu	Met	Ser	Leu	Ser	Asp	Cys	Leu	Asn	Arg	Ser	
				325					330					335		
Gly	Ser	Phe	Pro	Leu	Glu	Gln	Leu	Gln	Ser	Phe	Pro	Gln	Leu	Leu	Gln	
			340					345					350			
Asn	Ile	His	Cys	Leu	Glu	Leu	Pro	Ser	Gln	Met	Gly	Ser	Val	Leu	Asn	
		355					360					365				
Asn	Ser	Leu	Leu	Leu	His	Tyr	Ile	Asn	Cys	Val	Arg	Asp	Glu	Pro	Val	
		370				375					380					
Leu	Leu	Arg	Phe	His	Tyr	Trp	Leu	Ser	Gln	Thr	Leu	Gln	Glu	Glu	Cys	
385					390					395					400	
Ile	Trp	Tyr	Lys	Val	Asn	Asn	Tyr	Glu	His	Gly	Lys	Glu	Phe	Thr	Asn	
				405					410					415		
Phe	Leu	Asp	Thr	Ile	Ile	Arg	Ala	Glu	Cys	Phe	Leu	Gln	Glu	Gly	Tyr	
			420					425					430			
Tyr	Ser	Cys	Glu	Ala	Phe	Leu	Tyr	Lys	Ser	Leu	Pro	Leu	Trp	Asp	Gly	
		435					440					445				
Leu	Ser	Cys	Arg	Ser	Gln	Phe	Leu	Gln	Leu	Val	Ser	Trp	Ile	Pro	Phe	
	450					455					460					
Ser	Ser	Phe	Ser	Glu	Val	Lys	Pro	Leu	Leu	Phe	Asp	His	Leu	Ala	Gln	
465					470					475				480		
Leu	Phe	Phe	Thr	Ser	Thr	Ile	Tyr	Phe	Lys	Cys	Ser	Val	Leu	Gln	Ser	
				485					490					495		
Leu	Lys	Glu	Leu	Leu	Gln	Asn	Trp	Leu	Leu	Trp	Leu	Ser	Met	Asp	Ile	
			500					505					510			
His	Met	Lys	Pro	Val	Thr	Asn	Ser	Pro	Leu	Glu	Thr	Thr	Leu	Gly	Gly	
		515					520					525				
Ser	Met	Asn	Cys	Val	Ser	Lys	Leu	Ile	His	Tyr	Val	Gly	Trp	Leu	Ser	
	530						535					540				

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Thr Thr Ala Met Arg Leu Glu Ser Asn Asn Thr Phe Leu Leu His Phe
 545 550 555 560
 Ile Leu Asp Phe Tyr Glu Lys Val Cys Asp Ile Tyr Ile Asn Tyr Asp
 565 570 575
 Leu Pro Leu Val Val Leu Phe Pro Pro Gly Ile Phe Tyr Ser Ala Leu
 580 585 590
 Leu Ser Leu Asp Thr Ser Ile Leu Asn Gln Leu Cys Phe Ile Met His
 595 600 605
 Arg Tyr Arg Lys Asn Leu Thr Ala Ala Lys Lys Asn Glu Leu Val Gln
 610 615 620
 Lys Thr Lys Ser Glu Phe Asn Phe Ser Ser Lys Thr Tyr Gln Glu Phe
 625 630 635 640
 Asn Tyr Tyr Leu Thr Ser Met Val Gly Cys Leu Trp Thr Ser Lys Pro
 645 650 655
 Phe Ala Lys Gly Ile Tyr Ile Asp Pro Glu Ile Leu Glu Lys Thr Gly
 660 665 670
 Val Ala Glu Tyr Lys Asn Ser Leu Asn Val Val His His Pro Ser Phe
 675 680 685
 Leu Ser Tyr Ala Val Ser Phe Leu Leu Gln Glu Ser Pro Glu Glu Arg
 690 695 700
 Thr Val Asn Val Ser Ser Ile Arg Gly Lys Lys Trp Ser Trp Tyr Leu
 705 710 715 720
 Asp Tyr Leu Phe Ser Gln Gly Leu Gln Gly Leu Lys Leu Phe Ile Arg
 725 730 735
 Ser Ser Val His His Ser Ser Ile Pro Arg Ala Glu Gly Ile Asn Cys
 740 745 750
 Asn Asn Gln Tyr
 755

<210> 67
 <211> 504
 <212> PRT
 <213> Homo sapiens

<400> 67

Met Glu Ala Pro Leu Gln Thr Glu Met Val Glu Leu Val Pro Asn Gly
 1 5 10 15
 Lys His Ser Glu Gly Leu Leu Pro Val Ile Thr Pro Met Ala Gly Asn
 20 25 30
 Gln Arg Val Glu Asp Pro Ala Arg Ser Cys Met Glu Gly Lys Ser Phe
 35 40 45
 Leu Gln Lys Ser Pro Ser Lys Glu Pro His Phe Thr Asp Phe Glu Gly
 50 55 60

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Lys Thr Ser Phe Gly Met Ser Val Phe Asn Leu Ser Asn Ala Ile Met
 65 70 75 80
 Gly Ser Gly Ile Leu Gly Leu Ala Tyr Ala Met Ala Asn Thr Gly Ile
 85 90 95
 Ile Leu Phe Leu Phe Leu Leu Thr Ala Val Ala Leu Leu Ser Ser Tyr
 100 105 110
 Ser Ile His Leu Leu Leu Lys Ser Ser Gly Val Val Gly Ile Arg Ala
 115 120 125
 Tyr Glu Gln Leu Gly Tyr Arg Ala Phe Gly Thr Pro Gly Lys Leu Ala
 130 135 140
 Ala Ala Leu Ala Ile Thr Leu Gln Asn Ile Gly Ala Met Ser Ser Tyr
 145 150 155 160
 Leu Tyr Ile Ile Lys Ser Glu Leu Pro Leu Val Ile Gln Thr Phe Leu
 165 170 175
 Asn Leu Glu Glu Lys Thr Ser Asp Trp Tyr Met Asn Gly Asn Tyr Leu
 180 185 190
 Val Ile Leu Val Ser Val Thr Ile Ile Leu Pro Leu Ala Leu Met Arg
 195 200 205
 Gln Leu Gly Tyr Leu Gly Tyr Ser Ser Gly Phe Ser Leu Ser Cys Met
 210 215 220
 Val Phe Phe Leu Ile Ala Val Ile Tyr Lys Lys Phe His Val Pro Cys
 225 230 235 240
 Pro Leu Pro Pro Asn Phe Asn Asn Thr Thr Gly Asn Phe Ser His Val
 245 250 255
 Glu Ile Val Lys Glu Lys Val Gln Leu Gln Val Glu Pro Glu Ala Ser
 260 265 270
 Ala Phe Cys Thr Pro Ser Tyr Phe Thr Leu Asn Ser Gln Thr Ala Tyr
 275 280 285
 Thr Ile Pro Ile Met Ala Phe Ala Phe Val Cys His Pro Glu Val Leu
 290 295 300
 Pro Ile Tyr Thr Glu Leu Lys Asp Pro Ser Lys Lys Lys Met Gln His
 305 310 315 320
 Ile Ser Asn Leu Ser Ile Ala Val Met Tyr Ile Met Tyr Phe Leu Ala
 325 330 335
 Ala Leu Phe Gly Tyr Leu Thr Phe Tyr Asn Gly Val Glu Ser Glu Leu
 340 345 350
 Leu His Thr Tyr Ser Lys Val Asp Pro Phe Asp Val Leu Ile Leu Cys
 355 360 365
 Val Arg Val Ala Val Leu Thr Ala Val Thr Leu Thr Val Pro Ile Val
 370 375 380

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Leu Phe Pro Val Arg Arg Ala Ile Gln Gln Met Leu Phe Pro Asn Gln
 385 390 395 400

Glu Phe Ser Trp Leu Arg His Val Leu Ile Ala Val Gly Leu Leu Thr
 405 410 415

Cys Ile Asn Leu Leu Val Ile Phe Ala Pro Asn Ile Leu Gly Ile Phe
 420 425 430

Gly Val Ile Gly Ala Thr Ser Ala Pro Phe Leu Ile Phe Ile Phe Pro
 435 440 445

Ala Ile Phe Tyr Phe Arg Ile Met Pro Thr Glu Lys Glu Pro Ala Arg
 450 455 460

Ser Thr Pro Lys Ile Leu Ala Leu Cys Phe Ala Met Leu Gly Phe Leu
 465 470 475 480

Leu Met Thr Met Ser Leu Ser Phe Ile Ile Ile Asp Trp Ala Ser Gly
 485 490 495

Thr Ser Arg His Gly Gly Asn His
 500

<210> 68

<211> 145

<212> PRT

<213> Homo sapiens

<400> 68

Met Ala Thr Trp Ala Leu Leu Leu Leu Ala Ala Met Leu Leu Gly Asn
 1 5 10 15

Pro Gly Leu Val Phe Ser Arg Leu Ser Pro Glu Tyr Tyr Asp Leu Ala
 20 25 30

Arg Ala His Leu Arg Asp Glu Glu Lys Ser Cys Pro Cys Leu Ala Gln
 35 40 45

Glu Gly Pro Gln Gly Asp Leu Leu Thr Lys Thr Gln Glu Leu Gly Arg
 50 55 60

Asp Tyr Arg Thr Cys Leu Thr Ile Val Gln Lys Leu Lys Lys Met Val
 65 70 75 80

Asp Lys Pro Thr Gln Arg Ser Val Ser Asn Ala Ala Thr Arg Val Cys
 85 90 95

Arg Thr Gly Arg Ser Arg Trp Arg Asp Val Cys Arg Asn Phe Met Arg
 100 105 110

Arg Tyr Gln Ser Arg Val Ile Gln Gly Leu Val Ala Gly Glu Thr Ala
 115 120 125

Gln Gln Ile Cys Glu Asp Leu Arg Leu Cys Ile Pro Ser Thr Gly Pro
 130 135 140

Leu

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145

<210> 69
 <211> 128
 <212> PRT
 <213> Homo sapiens

<400> 69

Met	Trp	Ser	Thr	Arg	Ser	Pro	Asn	Ser	Thr	Ala	Trp	Pro	Leu	Ser	Leu
1				5					10					15	
Glu	Pro	Asp	Pro	Gly	Met	Ala	Ser	Ala	Ser	Thr	Thr	Met	His	Thr	Thr
			20					25					30		
Thr	Ile	Ala	Glu	Pro	Asp	Pro	Gly	Met	Ser	Gly	Trp	Pro	Asp	Gly	Arg
	35						40					45			
Met	Glu	Thr	Ser	Thr	Pro	Thr	Ile	Met	Asp	Ile	Val	Val	Ile	Ala	Gly
	50					55				60					
Val	Ile	Ala	Ala	Val	Ala	Ile	Val	Leu	Val	Ser	Leu	Leu	Phe	Val	Met
65					70				75						80
Leu	Arg	Tyr	Met	Tyr	Arg	His	Lys	Gly	Thr	Tyr	His	Thr	Asn	Glu	Ala
				85					90					95	
Lys	Gly	Thr	Glu	Phe	Ala	Glu	Ser	Ala	Asp	Ala	Ala	Leu	Gln	Gly	Asp
			100					105					110		
Pro	Ala	Leu	Gln	Asp	Ala	Gly	Asp	Ser	Ser	Arg	Lys	Glu	Tyr	Phe	Ile
		115					120					125			

<210> 70
 <211> 4861
 <212> PRT
 <213> Homo sapiens

<400> 70

Met	Ala	Thr	Met	Ile	Pro	Pro	Val	Lys	Leu	Lys	Trp	Leu	Glu	His	Leu
1				5					10					15	
Asn	Ser	Ser	Trp	Ile	Thr	Glu	Asp	Ser	Glu	Ser	Ile	Ala	Thr	Arg	Glu
			20					25					30		
Gly	Val	Ala	Val	Leu	Tyr	Ser	Lys	Leu	Val	Ser	Asn	Lys	Glu	Val	Val
		35					40					45			
Pro	Leu	Pro	Gln	Gln	Val	Leu	Cys	Leu	Lys	Gly	Pro	Gln	Leu	Pro	Asp
	50					55				60					
Phe	Glu	Arg	Glu	Ser	Leu	Ser	Ser	Asp	Glu	Gln	Asp	His	Tyr	Leu	Asp
65					70				75						80
Ala	Leu	Leu	Ser	Ser	Gln	Leu	Ala	Leu	Ala	Lys	Met	Val	Cys	Ser	Asp
				85				90						95	
Ser	Pro	Phe	Ala	Gly	Ala	Leu	Arg	Lys	Arg	Leu	Leu	Val	Leu	Gln	Arg
			100					105					110		

Val	Phe	Tyr	Ala	Leu	Ser	Asn	Lys	Tyr	His	Asp	Lys	Gly	Lys	Val	Lys
		115					120					125			
Gln	Gln	Gln	His	Ser	Pro	Glu	Ser	Ser	Ser	Gly	Ser	Ala	Asp	Val	His
	130					135					140				
Ser	Val	Ser	Glu	Arg	Pro	Arg	Ser	Ser	Thr	Asp	Ala	Leu	Ile	Glu	Met
145					150					155					160
Gly	Val	Arg	Thr	Gly	Leu	Ser	Leu	Leu	Phe	Ala	Leu	Leu	Arg	Gln	Ser
				165					170					175	
Trp	Met	Met	Pro	Val	Ser	Gly	Pro	Gly	Leu	Ser	Leu	Cys	Asn	Asp	Val
			180					185					190		
Ile	His	Thr	Ala	Ile	Glu	Val	Val	Ser	Ser	Leu	Pro	Pro	Leu	Ser	Leu
		195					200					205			
Ala	Asn	Glu	Ser	Lys	Ile	Pro	Pro	Met	Gly	Leu	Asp	Cys	Leu	Ser	Gln
	210					215					220				
Val	Thr	Thr	Phe	Leu	Lys	Gly	Val	Thr	Ile	Pro	Asn	Ser	Gly	Ala	Asp
225					230					235					240
Thr	Leu	Gly	Arg	Arg	Leu	Ala	Ser	Glu	Leu	Leu	Leu	Gly	Leu	Ala	Ala
				245					250					255	
Gln	Arg	Gly	Ser	Leu	Arg	Tyr	Leu	Leu	Glu	Trp	Ile	Glu	Met	Ala	Leu
			260					265					270		
Gly	Ala	Ser	Ala	Val	Val	His	Thr	Met	Glu	Lys	Gly	Lys	Leu	Leu	Ser
		275					280					285			
Ser	Gln	Glu	Gly	Met	Ile	Ser	Phe	Asp	Cys	Phe	Met	Thr	Ile	Leu	Met
	290					295					300				
Gln	Met	Arg	Arg	Ser	Leu	Gly	Ser	Ser	Ala	Asp	Arg	Ser	Gln	Trp	Arg
305					310					315					320
Glu	Pro	Thr	Arg	Thr	Ser	Asp	Gly	Leu	Cys	Ser	Leu	Tyr	Glu	Ala	Ala
				325					330					335	
Leu	Cys	Leu	Phe	Glu	Glu	Val	Cys	Arg	Met	Ala	Ser	Asp	Tyr	Ser	Arg
			340					345					350		
Thr	Cys	Ala	Ser	Pro	Asp	Ser	Ile	Gln	Thr	Gly	Asp	Ala	Pro	Ile	Val
		355					360					365			
Ser	Glu	Thr	Cys	Glu	Val	Tyr	Val	Trp	Gly	Ser	Asn	Ser	Ser	His	Gln
	370					375					380				
Leu	Val	Glu	Gly	Thr	Gln	Glu	Lys	Ile	Leu	Gln	Pro	Lys	Leu	Ala	Pro
385					390					395					400
Ser	Phe	Ser	Asp	Ala	Gln	Thr	Ile	Glu	Ala	Gly	Gln	Tyr	Cys	Thr	Phe
				405					410					415	
Val	Ile	Ser	Thr	Asp	Gly	Ser	Val	Arg	Ala	Cys	Gly	Lys	Gly	Ser	Tyr
			420					425					430		

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Gly Arg Leu Gly Leu Gly Asp Ser Asn Asn Gln Ser Thr Leu Lys Lys
 435 440 445
 Leu Thr Phe Glu Pro His Arg Ser Ile Lys Lys Val Ser Ser Ser Lys
 450 455 460
 Gly Ser Asp Gly His Thr Leu Ala Phe Thr Thr Glu Gly Glu Val Phe
 465 470 475 480
 Ser Trp Gly Asp Gly Asp Tyr Gly Lys Leu Gly His Gly Asn Ser Ser
 485 490 495
 Thr Gln Lys Tyr Pro Lys Leu Ile Gln Gly Pro Leu Gln Gly Lys Val
 500 505 510
 Val Val Cys Val Ser Ala Gly Tyr Arg His Ser Ala Ala Val Thr Glu
 515 520 525
 Asp Gly Glu Leu Tyr Thr Trp Gly Glu Gly Asp Phe Gly Arg Leu Gly
 530 535 540
 His Gly Asp Ser Asn Ser Arg Asn Ile Pro Thr Leu Val Lys Asp Ile
 545 550 555 560
 Ser Asn Val Gly Glu Val Ser Cys Gly Ser Ser His Thr Ile Ala Leu
 565 570 575
 Ser Lys Asp Gly Arg Thr Val Trp Ser Phe Gly Gly Gly Asp Asn Gly
 580 585 590
 Lys Leu Gly His Gly Asp Thr Asn Arg Val Tyr Lys Pro Lys Val Ile
 595 600 605
 Glu Ala Leu Gln Gly Met Phe Ile Arg Lys Val Cys Ala Gly Ser Gln
 610 615 620
 Ser Ser Leu Ala Leu Thr Ser Thr Gly Gln Val Tyr Ala Trp Gly Cys
 625 630 635 640
 Gly Ala Cys Leu Gly Cys Gly Ser Ser Glu Ala Thr Ala Leu Arg Pro
 645 650 655
 Lys Leu Ile Glu Glu Leu Ala Ala Thr Arg Ile Val Asp Val Ser Ile
 660 665 670
 Gly Asp Ser His Cys Leu Ala Leu Ser His Asp Asn Glu Val Tyr Ala
 675 680 685
 Trp Gly Asn Asn Ser Met Gly Gln Cys Gly Gln Gly Asn Ser Thr Gly
 690 695 700
 Pro Ile Thr Lys Pro Lys Lys Val Ser Gly Leu Asp Gly Ile Ala Ile
 705 710 715 720
 Gln Gln Ile Ser Ala Gly Thr Ser His Ser Leu Ala Trp Thr Ala Leu
 725 730 735
 Pro Arg Asp Arg Gln Val Val Ala Trp His Arg Pro Tyr Cys Val Asp
 740 745 750

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Leu Glu Glu Ser Thr Phe Ser His Leu Arg Ser Phe Leu Glu Arg Tyr
 755 760 765
 Cys Asp Lys Ile Asn Ser Glu Ile Pro Pro Leu Pro Phe Pro Ser Ser
 770 775 780
 Arg Glu His His Ser Phe Leu Lys Leu Cys Leu Lys Leu Leu Ser Asn
 785 790 795 800
 His Leu Ala Leu Ala Leu Ala Gly Gly Val Ala Thr Ser Ile Leu Gly
 805 810 815
 Arg Gln Ala Gly Pro Leu Arg Asn Leu Leu Phe Arg Leu Met Asp Ser
 820 825 830
 Thr Val Pro Asp Glu Ile Gln Glu Val Val Ile Glu Thr Leu Ser Val
 835 840 845
 Gly Ala Thr Met Leu Leu Pro Pro Leu Arg Glu Arg Met Glu Leu Leu
 850 855 860
 His Ser Leu Leu Pro Gln Gly Pro Asp Arg Trp Glu Ser Leu Ser Lys
 865 870 875 880
 Gly Gln Arg Met Gln Leu Asp Ile Ile Leu Thr Ser Leu Gln Asp His
 885 890 895
 Thr His Val Ala Ser Leu Leu Gly Tyr Ser Ser Pro Ser Asp Ala Ala
 900 905 910
 Asp Leu Ser Ser Val Cys Thr Gly Tyr Gly Asn Leu Ser Asp Gln Pro
 915 920 925
 Tyr Gly Thr Gln Ser Cys His Pro Asp Thr His Leu Ala Glu Ile Leu
 930 935 940
 Met Lys Thr Leu Leu Arg Asn Leu Gly Phe Tyr Thr Asp Gln Ala Phe
 945 950 955 960
 Gly Glu Leu Glu Lys Asn Ser Asp Lys Phe Leu Leu Gly Thr Ser Ser
 965 970 975
 Ser Glu Asn Ser Gln Pro Ala His Leu His Glu Leu Leu Cys Ser Leu
 980 985 990
 Gln Lys Gln Leu Leu Ala Phe Cys His Ile Asn Asn Ile Ser Glu Asn
 995 1000 1005
 Ser Ser Ser Val Ala Leu Leu His Lys His Leu Gln Leu Leu Leu
 1010 1015 1020
 Pro His Ala Thr Asp Ile Tyr Ser Arg Ser Ala Asn Leu Leu Lys
 1025 1030 1035
 Glu Ser Pro Trp Asn Gly Ser Val Gly Glu Lys Leu Arg Asp Val
 1040 1045 1050
 Ile Tyr Val Ser Ala Ala Gly Ser Met Leu Cys Gln Ile Val Asn
 1055 1060 1065

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Ser	Leu	Leu	Leu	Leu	Pro	Val	Ser	Val	Ala	Arg	Pro	Leu	Leu	Ser
1070						1075					1080			
Tyr	Leu	Leu	Asp	Leu	Leu	Pro	Pro	Leu	Asp	Cys	Leu	Asn	Arg	Leu
1085						1090					1095			
Leu	Pro	Ala	Ala	Asp	Leu	Leu	Glu	Asp	Gln	Glu	Leu	Gln	Trp	Pro
1100						1105					1110			
Leu	His	Gly	Gly	Pro	Glu	Leu	Ile	Asp	Pro	Ala	Gly	Leu	Pro	Leu
1115						1120					1125			
Pro	Gln	Pro	Ala	Gln	Ser	Trp	Val	Trp	Leu	Val	Asp	Leu	Glu	Arg
1130						1135					1140			
Thr	Ile	Ala	Leu	Leu	Ile	Gly	Arg	Cys	Leu	Gly	Gly	Met	Leu	Gln
1145						1150					1155			
Gly	Ser	Pro	Val	Ser	Pro	Glu	Glu	Gln	Asp	Thr	Ala	Tyr	Trp	Met
1160						1165					1170			
Lys	Thr	Pro	Leu	Phe	Ser	Asp	Gly	Val	Glu	Met	Asp	Thr	Pro	Gln
1175						1180					1185			
Leu	Asp	Lys	Cys	Met	Ser	Cys	Leu	Leu	Glu	Val	Ala	Leu	Ser	Gly
1190						1195					1200			
Asn	Glu	Glu	Gln	Lys	Pro	Phe	Asp	Tyr	Lys	Leu	Arg	Pro	Glu	Ile
1205						1210					1215			
Ala	Val	Tyr	Val	Asp	Leu	Ala	Leu	Gly	Cys	Ser	Lys	Glu	Pro	Ala
1220						1225					1230			
Arg	Ser	Leu	Trp	Ile	Ser	Met	Gln	Asp	Tyr	Ala	Val	Ser	Lys	Asp
1235						1240					1245			
Trp	Asp	Ser	Ala	Thr	Leu	Ser	Asn	Glu	Ser	Leu	Leu	Asp	Thr	Val
1250						1255					1260			
Ser	Arg	Phe	Val	Leu	Ala	Ala	Leu	Leu	Lys	His	Thr	Asn	Leu	Leu
1265						1270					1275			
Ser	Gln	Ala	Cys	Gly	Glu	Ser	Arg	Tyr	Gln	Pro	Gly	Lys	His	Leu
1280						1285					1290			
Ser	Glu	Val	Tyr	Arg	Cys	Val	Tyr	Lys	Val	Arg	Ser	Arg	Leu	Leu
1295						1300					1305			
Ala	Cys	Lys	Asn	Leu	Glu	Leu	Ile	Gln	Thr	Arg	Ser	Ser	Ser	Arg
1310						1315					1320			
Asp	Arg	Trp	Ile	Ser	Glu	Asn	Gln	Asp	Ser	Ala	Asp	Val	Asp	Pro
1325						1330					1335			
Gln	Glu	His	Ser	Phe	Thr	Arg	Thr	Ile	Asp	Glu	Glu	Ala	Glu	Met
1340						1345					1350			
Glu	Glu	Gln	Ala	Glu	Arg	Asp	Arg	Glu	Glu	Gly	His	Pro	Glu	Pro
1355						1360					1365			

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Glu Asp 1370	Glu Glu Glu Glu Arg 1375	Glu His Glu Val Met 1380	Thr Ala Gly
Lys Ile 1385	Phe Gln Cys Phe Leu 1390	Ser Ala Arg Glu Val 1395	Ala Arg Ser
Arg Asp 1400	Arg Asp Arg Met Asn 1405	Ser Gly Ala Gly Ser 1410	Gly Ala Arg
Ala Asp 1415	Asp Pro Pro Pro Gln 1420	Ser Gln Gln Glu Arg 1425	Arg Val Ser
Thr Asp 1430	Leu Pro Glu Gly Gln 1435	Asp Val Tyr Thr Ala 1440	Ala Cys Asn
Ser Val 1445	Ile His Arg Cys Ala 1450	Leu Leu Ile Leu Gly 1455	Val Ser Pro
Val Ile 1460	Asp Glu Leu Gln Lys 1465	Arg Arg Glu Glu Gly 1470	Gln Leu Gln
Gln Pro 1475	Ser Thr Ser Ala Ser 1480	Glu Gly Gly Gly Leu 1485	Met Thr Arg
Ser Glu 1490	Ser Leu Thr Ala Glu 1495	Ser Arg Leu Val His 1500	Thr Ser Pro
Asn Tyr 1505	Arg Leu Ile Lys Ser 1510	Arg Ser Glu Ser Asp 1515	Leu Ser Gln
Pro Glu 1520	Ser Asp Glu Glu Gly 1525	Tyr Ala Leu Ser Gly 1530	Arg Gln Asn
Val Asp 1535	Leu Asp Leu Ala Ala 1540	Ser His Arg Lys Arg 1545	Gly Pro Met
His Ser 1550	Gln Leu Glu Ser Leu 1555	Ser Asp Ser Trp Ala 1560	Arg Leu Lys
His Ser 1565	Arg Asp Trp Leu Cys 1570	Asn Ser Ser Tyr Ser 1575	Phe Glu Ser
Asp Phe 1580	Asp Leu Thr Lys Ser 1585	Leu Gly Val His Thr 1590	Leu Ile Glu
Asn Val 1595	Val Ser Phe Val Ser 1600	Gly Asp Val Gly Asn 1605	Ala Pro Gly
Phe Lys 1610	Glu Pro Glu Glu Ser 1615	Met Ser Thr Ser Pro 1620	Gln Ala Ser
Ile Ile 1625	Ala Met Glu Gln Gln 1630	Gln Leu Arg Ala Glu 1635	Leu Arg Leu
Glu Ala 1640	Leu His Gln Ile Leu 1645	Val Leu Leu Ser Gly 1650	Met Glu Glu
Lys Gly 1655	Ser Ile Ser Leu Ala 1660	Gly Ser Arg Leu Ser 1665	Ser Gly Phe

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Glu	Ser	Gly	Val	Glu	Asp	Asp	Gln	Met	Ala	Gln	Ile	Val	Glu	Arg
1970						1975					1980			
Leu	Phe	Ser	Leu	Leu	Ser	Asp	Cys	Met	Trp	Glu	Thr	Pro	Ile	Ala
1985						1990					1995			
Gln	Ala	Lys	His	Ala	Ile	Gln	Ile	Lys	Glu	Lys	Glu	Gln	Glu	Ile
2000						2005					2010			
Lys	Leu	Gln	Lys	Gln	Gly	Glu	Leu	Glu	Glu	Glu	Asp	Glu	Asn	Leu
2015						2020					2025			
Pro	Ile	Gln	Glu	Val	Ser	Phe	Asp	Pro	Glu	Lys	Ala	Gln	Cys	Cys
2030						2035					2040			
Leu	Val	Glu	Asn	Gly	Gln	Ile	Leu	Thr	His	Gly	Ser	Gly	Gly	Lys
2045						2050					2055			
Gly	Tyr	Gly	Leu	Ala	Ser	Thr	Gly	Val	Thr	Ser	Gly	Cys	Tyr	Gln
2060						2065					2070			
Trp	Lys	Phe	Tyr	Ile	Val	Lys	Glu	Asn	Arg	Gly	Asn	Glu	Gly	Thr
2075						2080					2085			
Cys	Val	Gly	Val	Ser	Arg	Trp	Pro	Val	His	Asp	Phe	Asn	His	Arg
2090						2095					2100			
Thr	Thr	Ser	Asp	Met	Trp	Leu	Tyr	Arg	Ala	Tyr	Ser	Gly	Asn	Leu
2105						2110					2115			
Tyr	His	Asn	Gly	Glu	Gln	Thr	Leu	Thr	Leu	Ser	Ser	Phe	Thr	Gln
2120						2125					2130			
Gly	Asp	Phe	Ile	Thr	Cys	Val	Leu	Asp	Met	Glu	Ala	Arg	Thr	Ile
2135						2140					2145			
Ser	Phe	Gly	Lys	Asn	Gly	Glu	Glu	Pro	Lys	Leu	Ala	Phe	Glu	Asp
2150						2155					2160			
Val	Asp	Ala	Ala	Glu	Leu	Tyr	Pro	Cys	Val	Met	Phe	Tyr	Ser	Ser
2165						2170					2175			
Asn	Pro	Gly	Glu	Lys	Val	Lys	Ile	Cys	Asp	Met	Gln	Met	Arg	Gly
2180						2185					2190			
Thr	Pro	Arg	Asp	Leu	Leu	Pro	Gly	Asp	Pro	Ile	Cys	Ser	Pro	Val
2195						2200					2205			
Ala	Ala	Val	Leu	Ala	Glu	Ala	Thr	Ile	Gln	Leu	Val	Arg	Ile	Leu
2210						2215					2220			
His	Arg	Thr	Asp	Arg	Trp	Thr	Tyr	Cys	Ile	Asn	Lys	Lys	Met	Met
2225						2230					2235			
Glu	Arg	Leu	His	Lys	Ile	Lys	Ile	Cys	Ile	Lys	Glu	Ser	Gly	Gln
2240						2245					2250			
Lys	Leu	Lys	Lys	Ser	Arg	Ser	Val	Gln	Ser	Arg	Glu	Glu	Asn	Glu
2255						2260					2265			

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Met	Arg	Glu	Glu	Lys	Glu	Ser	Lys	Glu	Glu	Glu	Lys	Gly	Lys	His
2270						2275					2280			
Thr	Arg	His	Gly	Leu	Ala	Asp	Leu	Ser	Glu	Leu	Gln	Leu	Arg	Thr
2285						2290					2295			
Leu	Cys	Ile	Glu	Val	Trp	Pro	Val	Leu	Ala	Val	Ile	Gly	Gly	Val
2300						2305					2310			
Asp	Ala	Gly	Leu	Arg	Val	Gly	Gly	Arg	Cys	Val	His	Lys	Gln	Thr
2315						2320					2325			
Gly	Arg	His	Ala	Thr	Leu	Leu	Gly	Val	Val	Lys	Glu	Gly	Ser	Thr
2330						2335					2340			
Ser	Ala	Lys	Val	Gln	Trp	Asp	Glu	Ala	Glu	Ile	Thr	Ile	Ser	Phe
2345						2350					2355			
Pro	Thr	Phe	Trp	Ser	Pro	Ser	Asp	Thr	Pro	Leu	Tyr	Asn	Leu	Glu
2360						2365					2370			
Pro	Cys	Glu	Pro	Leu	Pro	Phe	Asp	Val	Ala	Arg	Phe	Arg	Gly	Leu
2375						2380					2385			
Thr	Ala	Ser	Val	Leu	Leu	Asp	Leu	Thr	Tyr	Leu	Thr	Gly	Val	His
2390						2395					2400			
Glu	Asp	Met	Gly	Lys	Gln	Ser	Thr	Lys	Arg	His	Glu	Lys	Lys	His
2405						2410					2415			
Arg	His	Glu	Ser	Glu	Glu	Lys	Gly	Asp	Val	Glu	Gln	Lys	Pro	Glu
2420						2425					2430			
Ser	Glu	Ser	Ala	Leu	Asp	Met	Arg	Thr	Gly	Leu	Thr	Ser	Asp	Asp
2435						2440					2445			
Val	Lys	Ser	Gln	Ser	Thr	Thr	Ser	Ser	Lys	Ser	Glu	Asn	Glu	Ile
2450						2455					2460			
Ala	Ser	Phe	Ser	Leu	Asp	Pro	Thr	Leu	Pro	Ser	Val	Glu	Ser	Gln
2465						2470					2475			
His	Gln	Ile	Thr	Glu	Gly	Lys	Arg	Lys	Asn	His	Glu	His	Met	Ser
2480						2485					2490			
Lys	Asn	His	Asp	Val	Ala	Gln	Ser	Glu	Ile	Arg	Ala	Val	Gln	Leu
2495						2500					2505			
Ser	Tyr	Leu	Tyr	Leu	Gly	Ala	Met	Lys	Ser	Leu	Ser	Ala	Leu	Leu
2510						2515					2520			
Gly	Cys	Ser	Lys	Tyr	Ala	Glu	Leu	Leu	Leu	Ile	Pro	Lys	Val	Leu
2525						2530					2535			
Ala	Glu	Asn	Gly	His	Asn	Ser	Asp	Cys	Ala	Ser	Ser	Pro	Val	Val
2540						2545					2550			
His	Glu	Asp	Val	Glu	Met	Arg	Ala	Ala	Leu	Gln	Phe	Leu	Met	Arg
2555						2560					2565			

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His Met	Val Lys Arg Ala	Val Met Arg Ser Pro	Ile Lys Arg Ala
2570		2575	2580
Leu Gly	Leu Ala Asp Leu	Glu Arg Ala Gln Ala	Met Ile Tyr Lys
2585		2590	2595
Leu Val	Val His Gly Leu	Leu Glu Asp Gln Phe	Gly Gly Lys Ile
2600		2605	2610
Lys Gln	Glu Ile Asp Gln	Gln Ala Glu Glu Ser	Asp Pro Ala Gln
2615		2620	2625
Gln Ala	Gln Thr Pro Val	Thr Thr Ser Pro Ser	Ala Ser Ser Thr
2630		2635	2640
Thr Ser	Phe Met Ser Ser	Ser Leu Glu Asp Thr	Thr Thr Ala Thr
2645		2650	2655
Thr Pro	Val Thr Asp Thr	Glu Thr Val Pro Ala	Ser Glu Ser Pro
2660		2665	2670
Gly Val	Met Pro Leu Ser	Leu Leu Arg Gln Met	Phe Ser Ser Tyr
2675		2680	2685
Pro Thr	Thr Thr Val Leu	Pro Thr Arg Arg Ala	Gln Thr Pro Pro
2690		2695	2700
Ile Ser	Ser Leu Pro Thr	Ser Pro Ser Asp Glu	Val Gly Arg Arg
2705		2710	2715
Gln Ser	Leu Thr Ser Pro	Asp Ser Gln Ser Ala	Arg Pro Ala Asn
2720		2725	2730
Arg Thr	Ala Leu Ser Asp	Pro Ser Ser Arg Leu	Ser Thr Ser Pro
2735		2740	2745
Pro Pro	Pro Ala Ile Ala	Val Pro Leu Leu Glu	Met Gly Phe Ser
2750		2755	2760
Leu Arg	Gln Ile Ala Lys	Ala Met Glu Ala Thr	Gly Ala Arg Gly
2765		2770	2775
Glu Ala	Asp Ala Gln Asn	Ile Thr Val Leu Ala	Met Trp Met Ile
2780		2785	2790
Glu His	Pro Gly His Glu	Asp Glu Glu Glu Pro	Gln Ser Gly Ser
2795		2800	2805
Thr Ala	Asp Ser Arg Pro	Gly Ala Ala Val Leu	Gly Ser Gly Gly
2810		2815	2820
Lys Ser	Asn Asp Pro Cys	Tyr Leu Gln Ser Pro	Gly Asp Ile Pro
2825		2830	2835
Ser Ala	Asp Ala Ala Glu	Met Glu Glu Gly Phe	Ser Glu Ser Pro
2840		2845	2850
Asp Asn	Leu Asp His Thr	Glu Asn Ala Ala Ser	Gly Ser Gly Pro
2855		2860	2865

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Ser	Ala	Arg	Gly	Arg	Ser	Ala	Val	Thr	Arg	Arg	His	Lys	Phe	Asp
2870						2875					2880			
Leu	Ala	Ala	Arg	Thr	Leu	Leu	Ala	Arg	Ala	Ala	Gly	Leu	Tyr	Arg
2885						2890					2895			
Ser	Val	Gln	Ala	His	Arg	Asn	Gln	Ser	Arg	Arg	Glu	Gly	Ile	Ser
2900						2905					2910			
Leu	Gln	Gln	Asp	Pro	Gly	Ala	Leu	Tyr	Asp	Phe	Asn	Leu	Asp	Glu
2915						2920					2925			
Glu	Leu	Glu	Ile	Asp	Leu	Asp	Asp	Glu	Ala	Met	Glu	Ala	Met	Phe
2930						2935					2940			
Gly	Gln	Asp	Leu	Thr	Ser	Asp	Asn	Asp	Ile	Leu	Gly	Met	Trp	Ile
2945						2950					2955			
Pro	Glu	Val	Leu	Asp	Trp	Pro	Thr	Trp	His	Val	Cys	Glu	Ser	Glu
2960						2965					2970			
Asp	Arg	Glu	Glu	Val	Val	Val	Cys	Glu	Leu	Cys	Glu	Cys	Ser	Val
2975						2980					2985			
Val	Ser	Phe	Asn	Gln	His	Met	Lys	Arg	Asn	His	Pro	Gly	Cys	Gly
2990						2995					3000			
Arg	Ser	Ala	Asn	Arg	Gln	Gly	Tyr	Arg	Ser	Asn	Gly	Ser	Tyr	Val
3005						3010					3015			
Asp	Gly	Trp	Phe	Gly	Gly	Glu	Cys	Gly	Ser	Gly	Asn	Pro	Tyr	Tyr
3020						3025					3030			
Leu	Leu	Cys	Gly	Thr	Cys	Arg	Glu	Lys	Tyr	Leu	Ala	Met	Lys	Thr
3035						3040					3045			
Lys	Ser	Lys	Ser	Thr	Ser	Ser	Glu	Arg	Tyr	Lys	Gly	Gln	Ala	Pro
3050						3055					3060			
Asp	Leu	Ile	Gly	Lys	Gln	Asp	Ser	Val	Tyr	Glu	Glu	Asp	Trp	Asp
3065						3070					3075			
Met	Leu	Asp	Val	Asp	Glu	Asp	Glu	Lys	Leu	Thr	Gly	Glu	Glu	Glu
3080						3085					3090			
Phe	Glu	Leu	Leu	Ala	Gly	Pro	Leu	Gly	Leu	Asn	Asp	Arg	Arg	Ile
3095						3100					3105			
Val	Pro	Glu	Pro	Val	Gln	Phe	Pro	Asp	Ser	Asp	Pro	Leu	Gly	Ala
3110						3115					3120			
Ser	Val	Ala	Met	Val	Thr	Ala	Thr	Asn	Ser	Met	Glu	Glu	Thr	Leu
3125						3130					3135			
Met	Gln	Ile	Gly	Cys	His	Gly	Ser	Val	Glu	Lys	Ser	Ser	Ser	Gly
3140						3145					3150			
Arg	Ile	Thr	Leu	Gly	Glu	Gln	Ala	Ala	Ala	Leu	Ala	Asn	Pro	His
3155						3160					3165			

Asp	Arg	Val	Val	Ala	Leu	Arg	Arg	Val	Thr	Ala	Ala	Gln	Val
3170						3175					3180		
Leu	Leu	Ala	Arg	Thr	Met	Val	Met	Arg	Ala	Leu	Ser	Leu	Leu
3185						3190					3195		Ser
Val	Ser	Gly	Ser	Ser	Cys	Ser	Leu	Ala	Ala	Gly	Leu	Glu	Ser
3200						3205					3210		Leu
Gly	Leu	Thr	Asp	Ile	Arg	Thr	Leu	Val	Arg	Leu	Met	Cys	Leu
3215						3220					3225		Ala
Ala	Ala	Gly	Arg	Ala	Gly	Leu	Ser	Thr	Ser	Pro	Ser	Ala	Met
3230						3235					3240		Ala
Ser	Thr	Ser	Glu	Arg	Ser	Arg	Gly	Gly	His	Ser	Lys	Ala	Asn
3245						3250					3255		Lys
Pro	Ile	Ser	Cys	Leu	Ala	Tyr	Leu	Ser	Thr	Ala	Val	Gly	Cys
3260						3265					3270		Leu
Ala	Ser	Asn	Ala	Pro	Ser	Ala	Ala	Lys	Leu	Leu	Val	Gln	Leu
3275						3280					3285		Cys
Thr	Gln	Asn	Leu	Ile	Ser	Ala	Ala	Thr	Gly	Val	Asn	Leu	Thr
3290						3295					3300		Thr
Val	Asp	Asp	Ser	Ile	Gln	Arg	Lys	Phe	Leu	Pro	Ser	Phe	Leu
3305						3310					3315		Arg
Gly	Ile	Ala	Glu	Glu	Asn	Lys	Leu	Val	Thr	Ser	Pro	Asn	Phe
3320						3325					3330		Val
Val	Thr	Gln	Ala	Leu	Val	Ala	Leu	Leu	Ala	Asp	Lys	Gly	Ala
3335						3340					3345		Lys
Leu	Arg	Pro	Asn	Tyr	Asp	Lys	Ser	Glu	Val	Glu	Lys	Lys	Gly
3350						3355					3360		Pro
Leu	Glu	Leu	Ala	Asn	Ala	Leu	Ala	Ala	Cys	Cys	Leu	Ser	Ser
3365						3370					3375		Arg
Leu	Ser	Ser	Gln	His	Arg	Gln	Trp	Ala	Ala	Gln	Gln	Leu	Val
3380						3385					3390		Arg
Thr	Leu	Ala	Ala	His	Asp	Arg	Asp	Asn	Gln	Thr	Thr	Leu	Gln
3395						3400					3405		Thr
Leu	Ala	Asp	Met	Gly	Gly	Asp	Leu	Arg	Lys	Cys	Ser	Phe	Ile
3410						3415					3420		Lys
Leu	Glu	Ala	His	Gln	Asn	Arg	Val	Met	Thr	Cys	Val	Trp	Cys
3425						3430					3435		Asn
Lys	Lys	Gly	Leu	Leu	Ala	Thr	Ser	Gly	Asn	Asp	Gly	Thr	Ile
3440						3445					3450		Arg
Val	Trp	Asn	Val	Thr	Lys	Lys	Gln	Tyr	Ser	Leu	Gln	Gln	Thr
3455						3460					3465		Cys

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Val	Phe	Asn	Arg	Leu	Glu	Gly	Asp	Ala	Glu	Glu	Ser	Leu	Gly	Ser
3470						3475					3480			
Pro	Ser	Asp	Pro	Ser	Phe	Ser	Pro	Val	Ser	Trp	Ser	Ile	Ser	Gly
3485						3490					3495			
Lys	Tyr	Leu	Ala	Gly	Ala	Leu	Glu	Lys	Met	Val	Asn	Ile	Trp	Gln
3500						3505					3510			
Val	Asn	Gly	Gly	Lys	Gly	Leu	Val	Asp	Ile	Gln	Pro	His	Trp	Val
3515						3520					3525			
Ser	Ala	Leu	Ala	Trp	Pro	Glu	Glu	Gly	Pro	Ala	Thr	Ala	Trp	Ser
3530						3535					3540			
Gly	Glu	Ser	Pro	Glu	Leu	Leu	Leu	Val	Gly	Arg	Met	Asp	Gly	Ser
3545						3550					3555			
Leu	Gly	Leu	Ile	Glu	Val	Val	Asp	Val	Ser	Thr	Met	His	Arg	Arg
3560						3565					3570			
Glu	Leu	Glu	His	Cys	Tyr	Arg	Lys	Asp	Val	Ser	Val	Thr	Cys	Ile
3575						3580					3585			
Ala	Trp	Phe	Ser	Glu	Asp	Arg	Pro	Phe	Ala	Val	Gly	Tyr	Phe	Asp
3590						3595					3600			
Gly	Lys	Leu	Leu	Leu	Gly	Thr	Lys	Glu	Pro	Leu	Glu	Lys	Gly	Gly
3605						3610					3615			
Ile	Val	Leu	Ile	Asp	Ala	His	Lys	Asp	Thr	Leu	Ile	Ser	Met	Lys
3620						3625					3630			
Trp	Asp	Pro	Thr	Gly	His	Ile	Leu	Met	Thr	Cys	Ala	Lys	Glu	Asp
3635						3640					3645			
Ser	Val	Lys	Leu	Trp	Gly	Ser	Ile	Ser	Gly	Cys	Trp	Cys	Cys	Leu
3650						3655					3660			
His	Ser	Leu	Cys	His	Pro	Ser	Ile	Val	Asn	Gly	Ile	Ala	Trp	Cys
3665						3670					3675			
Arg	Leu	Pro	Gly	Lys	Gly	Ser	Lys	Leu	Gln	Leu	Leu	Met	Ala	Thr
3680						3685					3690			
Gly	Cys	Gln	Ser	Gly	Leu	Val	Cys	Val	Trp	Arg	Ile	Pro	Gln	Asp
3695						3700					3705			
Thr	Thr	Gln	Thr	Asn	Val	Thr	Ser	Ala	Glu	Gly	Trp	Trp	Asp	Gln
3710						3715					3720			
Glu	Ser	Asn	Cys	Gln	Asp	Gly	Tyr	Arg	Lys	Ser	Ser	Gly	Ala	Lys
3725						3730					3735			
Cys	Val	Tyr	Gln	Leu	Arg	Gly	His	Ile	Thr	Pro	Val	Arg	Thr	Val
3740						3745					3750			
Ala	Phe	Ser	Ser	Asp	Gly	Leu	Ala	Leu	Val	Ser	Gly	Gly	Leu	Gly
3755						3760					3765			

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Gly Leu Met Asn Ile Trp Ser Leu Arg Asp Gly Ser Val Leu Gln	3770	3775	3780
Thr Val Val Ile Gly Ser Gly Ala Ile Gln Thr Thr Val Trp Ile	3785	3790	3795
Pro Glu Val Gly Val Ala Ala Cys Ser Asn Arg Ser Lys Asp Val	3800	3805	3810
Leu Val Val Asn Cys Thr Ala Glu Trp Ala Ala Ala Asn His Val	3815	3820	3825
Leu Ala Thr Cys Arg Thr Ala Leu Lys Gln Gln Gly Val Leu Gly	3830	3835	3840
Leu Asn Met Ala Pro Cys Met Arg Ala Phe Leu Glu Arg Leu Pro	3845	3850	3855
Met Met Leu Gln Glu Gln Tyr Ala Tyr Glu Lys Pro His Val Val	3860	3865	3870
Cys Gly Asp Gln Leu Val His Ser Pro Tyr Met Gln Cys Leu Ala	3875	3880	3885
Ser Leu Ala Val Gly Leu His Leu Asp Gln Leu Leu Cys Asn Pro	3890	3895	3900
Pro Val Pro Pro His His Gln Asn Cys Leu Pro Asp Pro Ala Ser	3905	3910	3915
Trp Asn Pro Asn Glu Trp Ala Trp Leu Glu Cys Phe Ser Thr Thr	3920	3925	3930
Ile Lys Ala Ala Glu Ala Leu Thr Asn Gly Ala Gln Phe Pro Glu	3935	3940	3945
Ser Phe Thr Val Pro Asp Leu Glu Pro Val Pro Glu Asp Glu Leu	3950	3955	3960
Val Phe Leu Met Asp Asn Ser Lys Trp Ile Asn Gly Met Asp Glu	3965	3970	3975
Gln Ile Met Ser Trp Ala Thr Ser Arg Pro Glu Asp Trp His Leu	3980	3985	3990
Gly Gly Lys Cys Asp Val Tyr Leu Trp Gly Ala Gly Arg His Gly	3995	4000	4005
Gln Leu Ala Glu Ala Gly Arg Asn Val Met Val Pro Ala Ala Ala	4010	4015	4020
Pro Ser Phe Ser Gln Ala Gln Gln Val Ile Cys Gly Gln Asn Cys	4025	4030	4035
Thr Phe Val Ile Gln Ala Asn Gly Thr Val Leu Ala Cys Gly Glu	4040	4045	4050
Gly Ser Tyr Gly Arg Leu Gly Gln Gly Asn Ser Asp Asp Leu His	4055	4060	4065

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Val	Leu	Thr	Val	Ile	Ser	Ala	Leu	Gln	Gly	Phe	Val	Val	Thr	Gln
4070						4075					4080			
Leu	Val	Thr	Ser	Cys	Gly	Ser	Asp	Gly	His	Ser	Met	Ala	Leu	Thr
4085						4090					4095			
Glu	Ser	Gly	Glu	Val	Phe	Ser	Trp	Gly	Asp	Gly	Asp	Tyr	Gly	Lys
4100						4105					4110			
Leu	Gly	His	Gly	Asn	Ser	Asp	Arg	Gln	Arg	Arg	Pro	Arg	Gln	Ile
4115						4120					4125			
Glu	Ala	Leu	Gln	Gly	Glu	Glu	Val	Val	Gln	Met	Ser	Cys	Gly	Phe
4130						4135					4140			
Lys	His	Ser	Ala	Val	Val	Thr	Ser	Asp	Gly	Lys	Leu	Phe	Thr	Phe
4145						4150					4155			
Gly	Asn	Gly	Asp	Tyr	Gly	Arg	Leu	Gly	Leu	Gly	Asn	Thr	Ser	Asn
4160						4165					4170			
Lys	Lys	Leu	Pro	Glu	Arg	Val	Thr	Ala	Leu	Glu	Gly	Tyr	Gln	Ile
4175						4180					4185			
Gly	Gln	Val	Ala	Cys	Gly	Leu	Asn	His	Thr	Leu	Ala	Val	Ser	Ala
4190						4195					4200			
Asp	Gly	Ser	Met	Val	Trp	Ala	Phe	Gly	Asp	Gly	Asp	Tyr	Gly	Lys
4205						4210					4215			
Leu	Gly	Leu	Gly	Asn	Ser	Thr	Ala	Lys	Ser	Ser	Pro	Gln	Lys	Ile
4220						4225					4230			
Asp	Val	Leu	Cys	Gly	Ile	Gly	Ile	Lys	Lys	Val	Ala	Cys	Gly	Thr
4235						4240					4245			
Gln	Phe	Ser	Val	Ala	Leu	Thr	Lys	Asp	Gly	His	Val	Tyr	Thr	Phe
4250						4255					4260			
Gly	Gln	Asp	Arg	Leu	Ile	Gly	Leu	Pro	Glu	Gly	Arg	Ala	Arg	Asn
4265						4270					4275			
His	Asn	Arg	Pro	Gln	Gln	Ile	Pro	Val	Leu	Ala	Gly	Val	Ile	Ile
4280						4285					4290			
Glu	Asp	Val	Ala	Val	Gly	Ala	Glu	His	Thr	Leu	Ala	Leu	Ala	Ser
4295						4300					4305			
Asn	Gly	Asp	Val	Tyr	Ala	Trp	Gly	Ser	Asn	Ser	Glu	Gly	Gln	Leu
4310						4315					4320			
Gly	Leu	Gly	His	Thr	Asn	His	Val	Arg	Glu	Pro	Thr	Leu	Val	Thr
4325						4330					4335			
Gly	Leu	Gln	Gly	Lys	Asn	Val	Arg	Gln	Ile	Ser	Ala	Gly	Arg	Cys
4340						4345					4350			
His	Ser	Ala	Ala	Trp	Thr	Ala	Pro	Pro	Val	Pro	Pro	Arg	Ala	Pro
4355						4360					4365			

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Gly Gly Asn Ser Ile Pro Leu Thr Phe Ser Asn Arg Lys Glu Tyr
 4670 4675 4680
 Val Glu Arg Ala Ile Glu Tyr Arg Leu His Glu Met Asp Arg Gln
 4685 4690 4695
 Val Ala Ala Val Arg Glu Gly Met Ser Trp Ile Val Pro Val Pro
 4700 4705 4710
 Leu Leu Ser Leu Leu Thr Ala Lys Gln Leu Glu Gln Met Val Cys
 4715 4720 4725
 Gly Met Pro Glu Ile Ser Val Glu Val Leu Lys Lys Val Val Arg
 4730 4735 4740
 Tyr Arg Glu Val Asp Glu Gln His Gln Leu Val Gln Trp Phe Trp
 4745 4750 4755
 His Thr Leu Glu Glu Phe Ser Asn Glu Glu Arg Val Leu Phe Met
 4760 4765 4770
 Arg Phe Val Ser Gly Arg Ser Arg Leu Pro Ala Asn Thr Ala Asp
 4775 4780 4785
 Ile Ser Gln Arg Phe Gln Ile Met Lys Val Asp Arg Pro Tyr Asp
 4790 4795 4800
 Ser Leu Pro Thr Ser Gln Thr Cys Phe Phe Gln Leu Arg Leu Pro
 4805 4810 4815
 Pro Tyr Ser Ser Gln Leu Val Met Ala Glu Arg Leu Arg Tyr Ala
 4820 4825 4830
 Ile Asn Asn Cys Arg Ser Ile Asp Met Asp Asn Tyr Met Leu Ser
 4835 4840 4845
 Arg Asn Val Asp Asn Ala Glu Gly Ser Asp Thr Asp Tyr
 4850 4855 4860

<210> 71
 <211> 292
 <212> PRT
 <213> Homo sapiens

<400> 71

Met Ala Ser Ser Met Arg Ser Leu Phe Ser Asp His Gly Lys Tyr Val
 1 5 10 15
 Glu Ser Phe Arg Arg Phe Leu Asn His Ser Thr Glu His Gln Cys Met
 20 25 30
 Gln Glu Phe Met Asp Lys Lys Leu Pro Gly Ile Ile Gly Arg Ile Gly
 35 40 45
 Asp Thr Lys Ser Glu Ile Lys Ile Leu Ser Ile Gly Gly Gly Ala Gly
 50 55 60
 Glu Ile Asp Leu Gln Ile Leu Ser Lys Val Gln Ala Gln Tyr Pro Gly

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65		70		75		80
Val Cys Ile Asn Asn Glu Val Val Glu Pro Ser Ala Glu Gln Ile Ala						
		85		90		95
Lys Tyr Lys Glu Leu Val Ala Lys Thr Ser Asn Leu Glu Asn Val Lys						
		100		105		110
Phe Ala Trp His Lys Glu Thr Ser Ser Glu Tyr Gln Ser Arg Met Leu						
		115		120		125
Glu Lys Lys Glu Leu Gln Lys Trp Asp Phe Ile His Met Ile Gln Met						
		130		135		140
Leu Tyr Tyr Val Lys Asp Ile Pro Ala Thr Leu Lys Phe Phe His Ser						
		145		150		155
Leu Leu Gly Thr Asn Ala Lys Met Leu Ile Ile Val Val Ser Gly Ser						
		165		170		175
Ser Gly Trp Asp Lys Leu Trp Lys Lys Tyr Gly Ser Arg Phe Pro Gln						
		180		185		190
Asp Asp Leu Cys Gln Tyr Ile Thr Ser Asp Asp Leu Thr Gln Met Leu						
		195		200		205
Asp Asn Leu Gly Leu Lys Tyr Glu Cys Tyr Asp Leu Leu Ser Thr Met						
		210		215		220
Asp Ile Ser Asp Cys Phe Ile Asp Gly Asn Glu Asn Gly Asp Leu Leu						
		225		230		235
Trp Asp Phe Leu Thr Glu Thr Cys Asn Phe Asn Ala Thr Ala Pro Pro						
		245		250		255
Asp Leu Arg Ala Glu Leu Gly Lys Asp Leu Gln Glu Pro Glu Phe Ser						
		260		265		270
Ala Lys Lys Glu Gly Lys Val Leu Phe Asn Asn Thr Leu Ser Phe Ile						
		275		280		285
Val Ile Glu Ala						
		290				

<210> 72
 <211> 481
 <212> PRT
 <213> Homo sapiens

<400> 72

Met Ala Leu Ser Tyr Arg Val Ser Glu Leu Gln Ser Thr Ile Pro Glu			
1	5	10	15
His Ile Leu Gln Ser Thr Phe Val His Val Ile Ser Ser Asn Trp Ser			
	20	25	30
Gly Leu Gln Thr Glu Ser Ile Pro Glu Glu Met Lys Gln Ile Val Glu			
	35	40	45

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Glu Gln Gly Asn Lys Leu His Trp Ala Ala Leu Leu Ile Leu Met Val
 50 55 60
 Ile Ile Pro Thr Ile Gly Gly Asn Thr Leu Val Ile Leu Ala Val Ser
 65 70 75 80
 Leu Glu Lys Lys Leu Gln Tyr Ala Thr Asn Tyr Phe Leu Met Ser Leu
 85 90 95
 Ala Val Ala Asp Leu Leu Val Gly Leu Phe Val Met Pro Ile Ala Leu
 100 105 110
 Leu Thr Ile Met Phe Glu Ala Met Trp Pro Leu Pro Leu Val Leu Cys
 115 120 125
 Pro Ala Trp Leu Phe Leu Asp Val Leu Phe Ser Thr Ala Ser Ile Met
 130 135 140
 His Leu Cys Ala Ile Ser Val Asp Arg Tyr Ile Ala Ile Lys Lys Pro
 145 150 155 160
 Ile Gln Ala Asn Gln Tyr Asn Ser Arg Ala Thr Ala Phe Ile Lys Ile
 165 170 175
 Thr Val Val Trp Leu Ile Ser Ile Gly Ile Ala Ile Pro Val Pro Ile
 180 185 190
 Lys Gly Ile Glu Thr Asp Val Asp Asn Pro Asn Asn Ile Thr Cys Val
 195 200 205
 Leu Thr Lys Glu Arg Phe Gly Asp Phe Met Leu Phe Gly Ser Leu Ala
 210 215 220
 Ala Phe Phe Thr Pro Leu Ala Ile Met Ile Val Thr Tyr Phe Leu Thr
 225 230 235 240
 Ile His Ala Leu Gln Lys Lys Ala Tyr Leu Val Lys Asn Lys Pro Pro
 245 250 255
 Gln Arg Leu Thr Trp Leu Thr Val Ser Thr Val Phe Gln Arg Asp Glu
 260 265 270
 Thr Pro Cys Ser Ser Pro Glu Lys Val Ala Met Leu Asp Gly Ser Arg
 275 280 285
 Lys Asp Lys Ala Leu Pro Asn Ser Gly Asp Glu Thr Leu Met Arg Arg
 290 295 300
 Thr Ser Thr Ile Gly Lys Lys Ser Val Gln Thr Ile Ser Asn Glu Gln
 305 310 315 320
 Arg Ala Ser Lys Val Leu Gly Ile Val Phe Phe Leu Phe Leu Leu Met
 325 330 335
 Trp Cys Pro Phe Phe Ile Thr Asn Ile Thr Leu Val Leu Cys Asp Ser
 340 345 350
 Cys Asn Gln Thr Thr Leu Gln Met Leu Leu Glu Ile Phe Val Trp Ile
 355 360 365

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Gly Tyr Val Ser Ser Gly Val Asn Pro Leu Val Tyr Thr Leu Phe Asn
 370 375 380
 Lys Thr Phe Arg Asp Ala Phe Gly Arg Tyr Ile Thr Cys Asn Tyr Arg
 385 390 395 400
 Ala Thr Lys Ser Val Lys Thr Leu Arg Lys Arg Ser Ser Lys Ile Tyr
 405 410 415
 Phe Arg Asn Pro Met Ala Glu Asn Ser Lys Phe Phe Lys Lys His Gly
 420 425 430
 Ile Arg Asn Gly Ile Asn Pro Ala Met Tyr Gln Ser Pro Met Arg Leu
 435 440 445
 Arg Ser Ser Thr Ile Gln Ser Ser Ser Ile Ile Leu Leu Asp Thr Leu
 450 455 460
 Leu Leu Thr Glu Asn Glu Gly Asp Lys Thr Glu Glu Gln Val Ser Tyr
 465 470 475 480
 Val

<210> 73
 <211> 189
 <212> PRT
 <213> Homo sapiens

<400> 73

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
 1 5 10 15
 Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
 20 25 30
 Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
 35 40 45
 Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
 50 55 60
 Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
 65 70 75 80
 His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
 85 90 95
 Ser Ala Thr Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
 100 105 110
 Asn Gln Gln Leu Asn Asp Met Glu Ala Cys Val Ile Gln Glu Val Gly
 115 120 125
 Val Glu Glu Thr Pro Leu Met Asn Val Asp Ser Ile Leu Ala Val Lys
 130 135 140
 Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
 145 150 155 160

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Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
165 170 175

Leu Ser Lys Ile Phe Gln Glu Arg Leu Arg Arg Lys Glu
180 185

<210> 74

<211> 153

<212> PRT

<213> Homo sapiens

<400> 74

Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe
1 5 10 15

Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
20 25 30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
35 40 45

Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
50 55 60

Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly
65 70 75 80

Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys Cys
85 90 95

Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro Leu
100 105 110

Lys Pro Ala Lys Ser Ala Arg Ser Val Arg Ala Gln Arg His Thr Asp
115 120 125

Met Pro Lys Thr Gln Lys Glu Val His Leu Lys Asn Ala Ser Arg Gly
130 135 140

Ser Ala Gly. Asn Lys Asn Tyr Arg Met
145 150

<210> 75

<211> 632

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

 $\langle 222 \rangle \quad (199) \dots (199)$

<223> Xaa = any amino acid

<400> 75

Met Glu Thr Pro Ala Ala Ala Ala Pro Ala Gly Ser Leu Phe Pro Ser
1 5 10 15

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Phe Leu Leu Leu Ala Cys Gly Thr Leu Val Ala Ala Leu Leu Gly Ala
 20 25 30
 Ala His Arg Leu Gly Leu Phe Tyr Gln Leu Leu His Lys Val Asp Lys
 35 40 45
 Ala Ser Val Arg His Gly Gly Glu Asn Val Ala Ala Val Leu Arg Ala
 50 55 60
 His Gly Val Arg Phe Ile Phe Thr Leu Val Gly Gly His Ile Ser Pro
 65 70 75 80
 Leu Leu Val Ala Cys Glu Lys Leu Gly Ile Arg Val Val Asp Thr Arg
 85 90 95
 His Glu Val Thr Ala Val Phe Ala Ala Asp Ala Met Ala Arg Leu Ser
 100 105 110
 Gly Thr Val Gly Val Ala Ala Val Thr Ala Gly Pro Gly Leu Thr Asn
 115 120 125
 Thr Val Thr Ala Val Lys Asn Ala Gln Met Ala Gln Ser Pro Ile Leu
 130 135 140
 Leu Leu Gly Gly Ala Ala Ser Thr Leu Leu Gln Asn Arg Gly Ala Leu
 145 150 155 160
 Gln Ala Val Asp Gln Leu Ser Leu Phe Arg Pro Leu Cys Lys Phe Cys
 165 170 175
 Val Ser Val Arg Arg Val Arg Asp Ile Val Pro Thr Leu Arg Ala Ala
 180 185 190
 Met Ala Ala Ala Gln Ser Xaa Thr Pro Gly Pro Val Phe Val Glu Leu
 195 200 205
 Pro Val Asp Val Leu Tyr Pro Tyr Phe Met Val Gln Lys Glu Met Val
 210 215 220
 Pro Ala Lys Pro Pro Lys Gly Leu Val Gly Arg Val Val Ser Trp Tyr
 225 230 235 240
 Leu Glu Asn Tyr Leu Ala Asn Leu Phe Ala Gly Ala Trp Glu Pro Gln
 245 250 255
 Pro Glu Gly Pro Leu Pro Leu Asp Ile Pro Gln Ala Ser Pro Gln Gln
 260 265 270
 Val Gln Arg Cys Val Glu Ile Leu Ser Arg Ala Lys Arg Pro Leu Met
 275 280 285
 Val Leu Gly Ser Gln Ala Leu Leu Thr Pro Thr Ser Ala Asp Lys Leu
 290 295 300
 Arg Ala Ala Val Glu Thr Leu Gly Val Pro Cys Phe Leu Gly Gly Met
 305 310 315 320
 Ala Arg Gly Leu Leu Gly Arg Asn His Pro Leu His Ile Arg Glu Asn
 325 330 335

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Arg Ser Ala Ala Leu Lys Lys Ala Asp Val Ile Val Leu Ala Gly Thr
 340 345 350
 Val Cys Asp Phe Arg Leu Ser Tyr Gly Arg Val Leu Ser His Ser Ser
 355 360 365
 Lys Ile Ile Ile Val Asn Arg Asn Arg Glu Glu Met Leu Leu Asn Ser
 370 375 380
 Asp Ile Phe Trp Lys Pro Gln Glu Ala Val Gln Gly Asp Val Gly Ser
 385 390 395 400
 Phe Val Leu Lys Leu Val Glu Gly Leu Gln Gly Gln Thr Trp Ala Pro
 405 410 415
 Asp Trp Val Glu Glu Leu Arg Glu Ala Asp Arg Gln Lys Glu Gln Thr
 420 425 430
 Phe Arg Glu Lys Ala Ala Met Pro Val Ala Gln His Leu Asn Pro Val
 435 440 445
 Gln Val Leu Gln Leu Val Glu Glu Thr Leu Pro Asp Asn Ser Ile Leu
 450 455 460
 Val Val Asp Gly Gly Asp Phe Val Gly Thr Ala Ala His Leu Val Gln
 465 470 475 480
 Pro Arg Gly Pro Leu Arg Trp Leu Asp Pro Gly Ala Phe Gly Thr Leu
 485 490 495
 Gly Val Gly Ala Gly Phe Ala Leu Gly Ala Lys Leu Cys Arg Pro Asp
 500 505 510
 Ala Glu Val Trp Cys Leu Phe Gly Asp Gly Ala Phe Gly Tyr Ser Leu
 515 520 525
 Ile Glu Phe Asp Thr Phe Val Arg His Lys Ile Pro Val Met Ala Leu
 530 535 540
 Val Gly Asn Asp Ala Gly Trp Thr Gln Ile Ser Arg Glu Gln Val Pro
 545 550 555 560
 Ser Leu Gly Ser Asn Val Ala Cys Gly Leu Ala Tyr Thr Asp Tyr His
 565 570 575
 Lys Ala Ala Met Gly Leu Gly Ala Arg Gly Leu Leu Leu Ser Arg Glu
 580 585 590
 Asn Glu Asp Gln Val Val Lys Val Leu His Asp Ala Gln Gln Gln Cys
 595 600 605
 Arg Asp Gly His Pro Val Val Val Asn Ile Leu Ile Gly Arg Thr Asp
 610 615 620
 Phe Arg Asp Gly Ser Ile Ala Val
 625 630

<210> 76
 <211> 349
 <212> PRT

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<213> Homo sapiens

<400> 76

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Met Pro Val Glu Arg Met Arg Met Arg Pro Trp Leu Glu Glu Gln Ile
1           5           10           15

Asn Ser Asn Thr Ile Pro Gly Leu Lys Trp Leu Asn Lys Glu Lys Lys
20           25           30

Ile Phe Gln Ile Pro Trp Met His Ala Ala Arg His Gly Trp Asp Val
35           40           45

Glu Lys Asp Ala Pro Leu Phe Arg Asn Arg Ala Ile His Thr Gly Lys
50           55           60

His Gln Pro Gly Val Asp Lys Pro Asp Pro Lys Thr Trp Lys Ala Asn
65           70           75           80

Phe Arg Cys Ala Met Asn Ser Leu Pro Asp Ile Glu Glu Val Lys Asp
85           90           95

Lys Ser Ile Lys Lys Gly Asn Asn Ala Phe Arg Val Tyr Arg Met Leu
100          105          110

Pro Leu Ser Glu Arg Pro Ser Lys Lys Gly Lys Lys Pro Lys Thr Glu
115          120          125

Lys Glu Asp Lys Val Lys His Ile Lys Gln Glu Pro Val Glu Ser Ser
130          135          140

Leu Gly Leu Ser Asn Gly Val Ser Asp Leu Ser Pro Glu Tyr Ala Val
145          150          155          160

Leu Thr Ser Thr Ile Lys Asn Glu Val Asp Ser Thr Val Asn Ile Ile
165          170          175

Val Val Gly Gln Ser His Leu Asp Ser Asn Ile Glu Asn Gln Glu Ile
180          185          190

Val Thr Asn Pro Pro Asp Ile Cys Gln Val Val Glu Val Thr Thr Glu
195          200          205

Ser Asp Glu Gln Pro Val Ser Met Ser Glu Leu Tyr Pro Leu Gln Ile
210          215          220

Ser Pro Val Ser Ser Tyr Ala Glu Ser Glu Thr Thr Asp Ser Val Pro
225          230          235          240

Ser Asp Glu Glu Ser Ala Glu Gly Arg Pro His Trp Arg Lys Arg Asn
245          250          255

Ile Glu Gly Lys Gln Tyr Leu Ser Asn Met Gly Thr Arg Gly Ser Tyr
260          265          270

Leu Leu Pro Gly Met Ala Ser Phe Val Thr Ser Asn Lys Pro Asp Leu
275          280          285

Gln Val Thr Ile Lys Glu Glu Ser Asn Pro Val Pro Tyr Asn Ser Ser
290          295          300

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Trp Pro Pro Phe Gln Asp Leu Pro Leu Ser Ser Ser Met Thr Pro Ala
 305 310 315 320

Ser Ser Ser Ser Arg Pro Asp Arg Glu Thr Arg Ala Ser Val Ile Lys
 325 330 335

Lys Thr Ser Asp Ile Thr Gln Ala Arg Val Lys Ser Cys
 340 345

<210> 77

<211> 338

<212> PRT

<213> Homo sapiens

<400> 77

Met Ile Asn Ser Thr Ser Thr Gln Pro Pro Asp Glu Ser Cys Ser Gln
 1 5 10 15

Asn Leu Leu Ile Thr Gln Gln Ile Ile Pro Val Leu Tyr Cys Met Val
 20 25 30

Phe Ile Ala Gly Ile Leu Leu Asn Gly Val Ser Gly Trp Ile Phe Phe
 35 40 45

Tyr Val Pro Ser Ser Lys Ser Phe Ile Ile Tyr Leu Lys Asn Ile Val
 50 55 60

Ile Ala Asp Phe Val Met Ser Leu Thr Phe Pro Phe Lys Ile Leu Gly
 65 70 75 80

Asp Ser Gly Leu Gly Pro Trp Gln Leu Asn Val Phe Val Cys Arg Val
 85 90 95

Ser Ala Val Leu Phe Tyr Val Asn Met Tyr Val Ser Ile Val Phe Phe
 100 105 110

Gly Leu Ile Ser Phe Asp Arg Tyr Tyr Lys Ile Val Lys Pro Leu Trp
 115 120 125

Thr Ser Phe Ile Gln Ser Val Ser Tyr Ser Lys Leu Leu Ser Val Ile
 130 135 140

Val Trp Met Leu Met Leu Leu Leu Ala Val Pro Asn Ile Ile Leu Thr
 145 150 155 160

Asn Gln Ser Val Arg Glu Val Thr Gln Ile Lys Cys Ile Glu Leu Lys
 165 170 175

Ser Glu Leu Gly Arg Lys Trp His Lys Ala Ser Asn Tyr Ile Phe Val
 180 185 190

Ala Ile Phe Trp Ile Val Phe Leu Leu Leu Ile Val Phe Tyr Thr Ala
 195 200 205

Ile Thr Lys Lys Ile Phe Lys Ser His Leu Lys Ser Ser Arg Asn Ser
 210 215 220

Thr Ser Val Lys Lys Lys Ser Ser Arg Asn Ile Phe Ser Ile Val Phe

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225		230		235		240
Val Phe Phe Val	Cys Phe Val Pro Tyr His	Ile Ala Arg Ile	Pro Tyr			
	245	250	255			
Thr Lys Ser Gln	Thr Glu Ala His Tyr Ser Cys Gln	Ser Lys Glu Ile				
	260	265	270			
Leu Arg Tyr Met	Lys Glu Phe Thr Leu Leu Leu Ser	Ala Ala Asn Val				
	275	280	285			
Cys Leu Asp Pro	Ile Ile Tyr Phe Phe Leu Cys Gln	Pro Phe Arg Glu				
	290	295	300			
Ile Leu Cys Lys	Lys Leu His Ile Pro Leu Lys Ala Gln	Asn Asp Leu				
	305	310	315			320
Asp Ile Ser Arg	Ile Lys Arg Gly Asn Thr Thr Leu Glu	Ser Thr Asp				
	325	330	335			

Thr Leu

<210> 78
 <211> 232
 <212> PRT
 <213> Homo sapiens

<400> 78

Leu Glu Thr Gln	Ile Glu Ala Leu Lys Glu Glu Leu Leu Phe Met Lys
1	5 10 15
Lys Asn His Glu	Glu Glu Val Lys Gly Leu Gln Ala Gln Ile Ala Ser
	20 25 30
Ser Gly Leu Thr	Val Glu Val Asp Ala Pro Lys Ser Gln Asp Leu Ser
	35 40 45
Lys Ile Met Ala	Asp Ile Arg Ala Gln Tyr Asp Glu Leu Ala Arg Lys
	50 55 60
Asn Arg Glu Glu	Leu Asp Lys Tyr Trp Ser Gln Gln Ile Glu Glu Ser
	65 70 75 80
Thr Thr Val Val	Thr Thr Gln Ser Ala Glu Val Gly Ala Ala Glu Thr
	85 90 95
Thr Leu Thr Glu	Leu Arg Arg Thr Val Gln Ser Leu Glu Ile Arg Leu
	100 105 110
Asp Arg Met Arg	Asn Leu Lys Ala Ser Leu Glu Asn Ser Leu Arg Glu
	115 120 125
Val Glu Ala Arg	Tyr Ala Leu Gln Met Glu Gln Leu Asn Gly Ile Leu
	130 135 140
Leu His Leu Glu	Ser Glu Leu Ala Gln Thr Arg Ala Glu Gly Gln Arg
	145 150 155 160

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Gln Ala Gln Glu Tyr Glu Ala Leu Leu Asn Ile Lys Val Lys Leu Glu
 165 170 175

Ala Glu Ile Ala Thr Tyr Arg Arg Leu Leu Glu Asp Gly Glu Asp Phe
 180 185 190

Asn Leu Gly Asp Ala Leu Asp Ser Ser Asn Ser Met Gln Thr Ile Gln
 195 200 205

Lys Thr Thr Thr Arg Arg Ile Val Asp Gly Lys Val Val Ser Glu Thr
 210 215 220

Asn Asp Thr Lys Val Leu Arg His
 225 230

<210> 79

<211> 483

<212> PRT

<213> Homo sapiens

<400> 79

Met Ser Ile Arg Val Thr Gln Lys Ser Tyr Lys Val Ser Thr Ser Gly
 1 5 10 15

Pro Arg Ala Phe Ser Ser Arg Ser Tyr Thr Ser Gly Pro Gly Ser Arg
 20 25 30

Ile Ser Ser Ser Ser Phe Ser Arg Val Gly Ser Ser Asn Phe Arg Gly
 35 40 45

Gly Leu Gly Gly Gly Tyr Gly Gly Ala Ser Gly Met Gly Gly Ile Thr
 50 55 60

Ala Val Thr Val Asn Gln Ser Leu Leu Ser Pro Leu Val Leu Glu Val
 65 70 75 80

Asp Pro Asn Ile Gln Ala Val Arg Thr Gln Glu Lys Glu Gln Ile Lys
 85 90 95

Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
 100 105 110

Glu Gln Gln Asn Lys Met Leu Glu Thr Lys Trp Ser Leu Leu Gln Gln
 115 120 125

Gln Lys Thr Ala Arg Ser Asn Met Asp Asn Met Phe Glu Ser Tyr Ile
 130 135 140

Asn Asn Leu Arg Arg Gln Leu Glu Thr Leu Gly Gln Glu Lys Leu Lys
 145 150 155 160

Leu Glu Ala Glu Leu Gly Asn Met Gln Gly Leu Val Glu Asp Phe Lys
 165 170 175

Asn Lys Tyr Glu Asp Glu Ile Asn Lys Arg Thr Glu Met Glu Asn Glu
 180 185 190

Phe Val Leu Ile Lys Lys Asp Val Asp Glu Ala Tyr Met Asn Lys Val
 195 200 205

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Glu Leu Glu Ser Arg Leu Glu Gly Leu Thr Asp Glu Ile Asn Phe Leu
 210 215 220
 Arg Gln Leu Tyr Glu Glu Glu Ile Arg Glu Leu Gln Ser Gln Ile Ser
 225 230 235 240
 Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp Met
 245 250 255
 Asp Ser Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Asp Ile Ala Asn
 260 265 270
 Arg Ser Arg Ala Glu Ala Glu Ser Met Tyr Gln Ile Lys Tyr Glu Glu
 275 280 285
 Leu Gln Ser Leu Ala Gly Lys His Gly Asp Asp Leu Arg Arg Thr Lys
 290 295 300
 Thr Glu Ile Ser Glu Met Asn Arg Asn Ile Ser Arg Leu Gln Ala Glu
 305 310 315 320
 Ile Glu Gly Leu Lys Gly Gln Arg Ala Ser Leu Glu Ala Ala Ile Ala
 325 330 335
 Asp Ala Glu Gln Arg Gly Glu Leu Ala Ile Lys Asp Ala Asn Ala Lys
 340 345 350
 Leu Ser Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala
 355 360 365
 Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Asn Val Lys Leu Ala Leu
 370 375 380
 Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser
 385 390 395 400
 Arg Leu Glu Ser Gly Met Gln Asn Met Ser Ile His Thr Lys Thr Thr
 405 410 415
 Ser Gly Tyr Ala Gly Gly Leu Ser Ser Ala Tyr Gly Gly Leu Thr Ser
 420 425 430
 Pro Gly Leu Ser Tyr Ser Leu Gly Ser Ser Phe Gly Ser Gly Ala Gly
 435 440 445
 Ser Ser Ser Phe Ser Arg Thr Ser Ser Ser Arg Ala Val Val Val Lys
 450 455 460
 Lys Ile Glu Thr Arg Asp Gly Lys Leu Val Ser Glu Ser Ser Asp Val
 465 470 475 480
 Leu Pro Lys

<210> 80
 <211> 440
 <212> PRT
 <213> Homo sapiens

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<400> 80

Met Gly Pro Pro Gly Ser Pro Trp Gln Trp Val Thr Leu Leu Leu Gly
 1 5 10 15
 Leu Leu Leu Pro Pro Ala Ala Pro Phe Trp Leu Leu Asn Val Leu Phe
 20 25 30
 Pro Pro His Thr Thr Pro Lys Ala Glu Leu Ser Asn His Thr Arg Pro
 35 40 45
 Val Ile Leu Val Pro Gly Cys Leu Gly Asn Gln Leu Glu Ala Lys Leu
 50 55 60
 Asp Lys Pro Asp Val Val Asn Trp Met Cys Tyr Arg Lys Thr Glu Asp
 65 70 75 80
 Phe Phe Thr Ile Trp Leu Asp Leu Asn Met Phe Leu Pro Leu Gly Val
 85 90 95
 Asp Cys Trp Ile Asp Asn Thr Arg Val Val Tyr Asn Arg Ser Ser Gly
 100 105 110
 Leu Val Ser Asn Ala Pro Gly Val Gln Ile Arg Val Pro Gly Phe Gly
 115 120 125
 Lys Thr Tyr Ser Val Glu Tyr Leu Asp Ser Ser Lys Leu Ala Gly Tyr
 130 135 140
 Leu His Thr Leu Val Gln Asn Leu Val Asn Asn Gly Tyr Val Arg Asp
 145 150 155 160
 Glu Thr Val Arg Ala Ala Pro Tyr Asp Trp Arg Leu Glu Pro Gly Gln
 165 170 175
 Gln Glu Glu Tyr Tyr Arg Lys Leu Ala Gly Leu Val Glu Glu Met His
 180 185 190
 Ala Ala Tyr Gly Lys Pro Val Phe Leu Ile Gly His Ser Leu Gly Cys
 195 200 205
 Leu His Leu Leu Tyr Phe Leu Leu Arg Gln Pro Gln Ala Trp Lys Asp
 210 215 220
 Arg Phe Ile Asp Gly Phe Ile Ser Leu Gly Ala Pro Trp Gly Gly Ser
 225 230 235 240
 Ile Lys Pro Met Leu Val Leu Ala Ser Gly Asp Asn Gln Gly Ile Pro
 245 250 255
 Ile Met Ser Ser Ile Lys Leu Lys Glu Glu Gln Arg Ile Thr Thr Thr
 260 265 270
 Ser Pro Trp Met Phe Pro Ser Arg Met Ala Trp Pro Glu Asp His Val
 275 280 285
 Phe Ile Ser Thr Pro Ser Phe Asn Tyr Thr Gly Arg Asp Phe Gln Arg
 290 295 300
 Phe Phe Ala Asp Leu His Phe Glu Glu Gly Trp Tyr Met Trp Leu Gln

[illegible]

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<210> 82
 <211> 314
 <212> PRT
 <213> Homo sapiens

<400> 82

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Met Ala Pro Pro Gln Val Leu Ala Phe Gly Leu Leu Leu Ala Ala Ala
1           5           10           15

Thr Ala Thr Phe Ala Ala Ala Gln Glu Glu Cys Val Cys Glu Asn Tyr
20           25           30

Lys Leu Ala Val Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys
35           40           45

Thr Ser Val Gly Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala
50           55           60

Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg
65           70           75           80

Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp
85           90           95

Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly
100          105          110

Thr Ser Thr Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp
115          120          125

Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile
130          135          140

Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys
145          150          155          160

Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu
165          170          175

Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr
180          185          190

Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp
195          200          205

Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser
210          215          220

Leu Phe His Ser Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu
225          230          235          240

Asp Leu Asp Pro Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala
245          250          255

Pro Glu Phe Ser Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile
260          265          270

Val Val Val Val Ile Ala Val Val Ala Gly Ile Val Val Leu Val Ile
275          280          285

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Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu
 290 295 300

Met Gly Glu Met His Arg Glu Leu Asn Ala
 305 310

<210> 83

<211> 720

<212> PRT

<213> Homo sapiens

<400> 83

Lys Ser Val Trp Lys Gly Gly Leu Arg Glu Arg Asp Pro Arg Gly Thr
 1 5 10 15

Arg Gly Gly Gly Arg Arg Gly Thr Gly Ser Gln Pro Ala Leu Cys Leu
 20 25 30

Gly Ala Gly Arg Gln Glu Gly Ala Met Ala Leu Asp Gly Ile Arg Met
 35 40 45

Pro Asp Gly Cys Tyr Ala Asp Gly Thr Trp Glu Leu Ser Val His Val
 50 55 60

Thr Asp Leu Asn Arg Asp Ile Thr Leu Arg Val Thr Gly Glu Val His
 65 70 75 80

Ile Gly Gly Val Met Leu Lys Leu Val Glu Lys Leu Asp Val Lys Lys
 85 90 95

Asp Trp Ser Asp His Ala Leu Trp Trp Glu Lys Lys Arg Thr Trp Leu
 100 105 110

Leu Lys Thr His Trp Thr Leu Asp Lys Tyr Gly Ile Gln Ala Asp Ala
 115 120 125

Lys Leu Gln Phe Thr Pro Gln His Lys Leu Leu Arg Leu Gln Leu Pro
 130 135 140

Asn Met Lys Tyr Val Lys Val Lys Val Asn Phe Ser Asp Arg Val Phe
 145 150 155 160

Lys Ala Val Ser Asp Ile Cys Lys Thr Phe Asn Ile Arg His Pro Glu
 165 170 175

Glu Leu Ser Leu Leu Lys Lys Pro Arg Asp Pro Thr Lys Lys Lys Lys
 180 185 190

Lys Lys Leu Asp Asp Gln Ser Glu Asp Glu Ala Leu Glu Leu Glu Gly
 195 200 205

Pro Leu Ile Thr Pro Gly Ser Gly Ser Ile Tyr Ser Ser Pro Gly Leu
 210 215 220

Tyr Ser Lys Thr Met Thr Pro Thr Tyr Asp Ala His Asp Gly Ser Pro
 225 230 235 240

Leu Ser Pro Thr Ser Ala Trp Phe Gly Asp Ser Ala Leu Ser Glu Gly

245

250

255

Asn	Pro	Gly	Ile	Leu	Ala	Val	Ser	Gln	Pro	Ile	Thr	Ser	Pro	Glu	Ile	
			260							265				270		
Leu	Ala	Lys	Met	Phe	Lys	Pro	Gln	Ala	Leu	Leu	Asp	Lys	Ala	Lys	Ile	
			275							280				285		
Asn	Gln	Gly	Trp	Leu	Asp	Ser	Ser	Arg	Ser	Leu	Met	Glu	Gln	Asp	Val	
			290							295				300		
Lys	Glu	Asn	Glu	Ala	Leu	Leu	Leu	Arg	Phe	Lys	Tyr	Tyr	Ser	Phe	Phe	
			305							310				320		
Asp	Leu	Asn	Pro	Lys	Tyr	Asp	Ala	Ile	Arg	Ile	Asn	Gln	Leu	Tyr	Glu	
			325							330				335		
Gln	Ala	Lys	Trp	Ala	Ile	Leu	Leu	Glu	Glu	Ile	Glu	Cys	Thr	Glu	Glu	
			340							345				350		
Glu	Met	Met	Met	Phe	Ala	Ala	Leu	Gln	Tyr	His	Ile	Asn	Lys	Leu	Ser	
			355							360				365		
Ile	Met	Thr	Ser	Glu	Asn	His	Leu	Asn	Asn	Ser	Asp	Lys	Glu	Val	Asp	
			370							375				380		
Glu	Val	Asp	Ala	Ala	Leu	Ser	Asp	Leu	Glu	Ile	Thr	Leu	Glu	Gly	Gly	
			385							390				400		
Lys	Thr	Ser	Thr	Ile	Leu	Gly	Asp	Ile	Thr	Ser	Ile	Pro	Glu	Leu	Ala	
			405							410				415		
Asp	Tyr	Ile	Lys	Val	Phe	Lys	Pro	Lys	Lys	Leu	Thr	Leu	Lys	Gly	Tyr	
			420							425				430		
Lys	Gln	Tyr	Trp	Cys	Thr	Phe	Lys	Asp	Thr	Ser	Ile	Ser	Cys	Tyr	Lys	
			435							440				445		
Ser	Lys	Glu	Glu	Ser	Ser	Gly	Thr	Pro	Ala	His	Gln	Met	Asn	Leu	Arg	
			450							455				460		
Gly	Cys	Glu	Val	Thr	Pro	Asp	Val	Asn	Ile	Ser	Gly	Gln	Lys	Phe	Asn	
			465							470				480		
Ile	Lys	Leu	Leu	Ile	Pro	Val	Ala	Glu	Gly	Met	Asn	Glu	Ile	Trp	Leu	
			485							490				495		
Arg	Cys	Asp	Asn	Glu	Lys	Gln	Tyr	Ala	His	Trp	Met	Ala	Ala	Cys	Arg	
			500							505				510		
Leu	Ala	Ser	Lys	Gly	Lys	Thr	Met	Ala	Asp	Ser	Ser	Tyr	Asn	Leu	Glu	
			515							520				525		
Val	Gln	Asn	Ile	Leu	Ser	Phe	Leu	Lys	Met	Gln	His	Leu	Asn	Pro	Asp	
			530							535				540		
Pro	Gln	Leu	Ile	Pro	Glu	Gln	Ile	Thr	Thr	Asp	Ile	Thr	Pro	Glu	Cys	
			545							550				560		
Leu	Val	Ser	Pro	Arg	Tyr	Leu	Lys	Lys	Tyr	Lys	Asn	Lys	Gln	Ile	Thr	

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565 570 575
 Ala Arg Ile Leu Glu Ala His Gln Asn Val Ala Gln Met Ser Leu Ile
 580 585 590
 Glu Ala Lys Met Arg Phe Ile Gln Ala Trp Gln Ser Leu Pro Glu Phe
 595 600 605
 Gly Ile Thr His Phe Ile Ala Arg Phe Gln Gly Gly Lys Lys Glu Glu
 610 615 620
 Leu Ile Gly Ile Ala Tyr Asn Arg Leu Ile Arg Met Asp Ala Ser Thr
 625 630 635 640
 Gly Asp Ala Ile Lys Thr Trp Arg Phe Ser Asn Met Lys Gln Trp Asn
 645 650 655
 Val Asn Trp Glu Ile Lys Met Val Thr Val Glu Phe Ala Asp Glu Val
 660 665 670
 Arg Leu Ser Phe Ile Cys Thr Glu Val Asp Cys Lys Val Val His Glu
 675 680 685
 Phe Ile Gly Gly Tyr Ile Phe Leu Ser Thr Arg Ala Lys Asp Gln Asn
 690 695 700
 Glu Ser Leu Asp Glu Glu Met Phe Tyr Lys Leu Thr Ser Gly Trp Val
 705 710 715 720

 <210> 84
 <211> 582
 <212> PRT
 <213> Homo sapiens

 <400> 84

 Met Ser Pro Ala Pro Arg Pro Pro Arg Cys Leu Leu Leu Pro Leu Leu
 1 5 10 15
 Thr Leu Gly Thr Ala Leu Ala Ser Leu Gly Ser Ala Gln Ser Ser Ser
 20 25 30
 Phe Ser Pro Glu Ala Trp Leu Gln Gln Tyr Gly Tyr Leu Pro Pro Gly
 35 40 45
 Asp Leu Arg Thr His Thr Gln Arg Ser Pro Gln Ser Leu Ser Ala Ala
 50 55 60
 Ile Ala Ala Met Gln Lys Phe Tyr Gly Leu Gln Val Thr Gly Lys Ala
 65 70 75 80
 Asp Ala Asp Thr Met Lys Ala Met Arg Arg Pro Arg Cys Gly Val Pro
 85 90 95
 Asp Lys Phe Gly Ala Glu Ile Lys Ala Asn Val Arg Arg Lys Arg Tyr
 100 105 110
 Ala Ile Gln Gly Leu Lys Trp Gln His Asn Glu Ile Thr Phe Cys Ile
 115 120 125

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Gln Asn Tyr Thr Pro Lys Val Gly Glu Tyr Ala Thr Tyr Glu Ala Ile
 130 135 140
 Arg Lys Ala Phe Arg Val Trp Glu Ser Ala Thr Pro Leu Arg Phe Arg
 145 150 155 160
 Glu Val Pro Tyr Ala Tyr Ile Arg Glu Gly His Glu Lys Gln Ala Asp
 165 170 175
 Ile Met Ile Phe Phe Ala Glu Gly Phe His Gly Asp Ser Thr Pro Phe
 180 185 190
 Asp Gly Glu Gly Gly Phe Leu Ala His Ala Tyr Phe Pro Gly Pro Asn
 195 200 205
 Ile Gly Gly Asp Thr His Phe Asp Ser Ala Glu Pro Trp Thr Val Arg
 210 215 220
 Asn Glu Asp Leu Asn Gly Asn Asp Ile Phe Leu Val Ala Val His Glu
 225 230 235 240
 Leu Gly His Ala Leu Gly Leu Glu His Ser Ser Asp Pro Ser Ala Ile
 245 250 255
 Met Ala Pro Phe Tyr Gln Trp Met Asp Thr Glu Asn Phe Val Leu Pro
 260 265 270
 Asp Asp Asp Arg Arg Gly Ile Gln Gln Leu Tyr Gly Gly Glu Ser Gly
 275 280 285
 Phe Pro Thr Lys Met Pro Pro Gln Pro Arg Thr Thr Ser Arg Pro Ser
 290 295 300
 Val Pro Asp Lys Pro Lys Asn Pro Thr Tyr Gly Pro Asn Ile Cys Asp
 305 310 315 320
 Gly Asn Phe Asp Thr Val Ala Met Leu Arg Gly Glu Met Phe Val Phe
 325 330 335
 Lys Glu Arg Trp Phe Trp Arg Val Arg Asn Asn Gln Val Met Asp Gly
 340 345 350
 Tyr Pro Met Pro Ile Gly Gln Phe Trp Arg Gly Leu Pro Ala Ser Ile
 355 360 365
 Asn Thr Ala Tyr Glu Arg Lys Asp Gly Lys Phe Val Phe Phe Lys Gly
 370 375 380
 Asp Lys His Trp Val Phe Asp Glu Ala Ser Leu Glu Pro Gly Tyr Pro
 385 390 395 400
 Lys His Ile Lys Glu Leu Gly Arg Gly Leu Pro Thr Asp Lys Ile Asp
 405 410 415
 Ala Ala Leu Phe Trp Met Pro Asn Gly Lys Thr Tyr Phe Phe Arg Gly
 420 425 430
 Asn Lys Tyr Tyr Arg Phe Asn Glu Glu Leu Arg Ala Val Asp Ser Glu
 435 440 445

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Tyr Pro Lys Asn Ile Lys Val Trp Glu Gly Ile Pro Glu Ser Pro Arg
 450 455 460
 Gly Ser Phe Met Gly Ser Asp Glu Val Phe Thr Tyr Phe Tyr Lys Gly
 465 470 475 480
 Asn Lys Tyr Trp Lys Phe Asn Asn Gln Lys Leu Lys Val Glu Pro Gly
 485 490 495
 Tyr Pro Lys Ser Ala Leu Arg Asp Trp Met Gly Cys Pro Ser Gly Gly
 500 505 510
 Arg Pro Asp Glu Gly Thr Glu Glu Glu Thr Glu Val Ile Ile Ile Glu
 515 520 525
 Val Asp Glu Glu Gly Gly Gly Ala Val Ser Ala Ala Ala Val Val Leu
 530 535 540
 Pro Val Leu Leu Leu Leu Leu Val Leu Ala Val Gly Leu Ala Val Phe
 545 550 555 560
 Phe Phe Arg Arg His Gly Thr Pro Arg Arg Leu Leu Tyr Cys Gln Arg
 565 570 575
 Ser Leu Leu Asp Lys Val
 580

<210> 85
 <211> 1246
 <212> PRT
 <213> Homo sapiens

<400> 85

Met Leu Ala Ser Ser Ser Arg Ile Arg Ala Ala Trp Thr Arg Ala Leu
 1 5 10 15
 Leu Leu Pro Leu Leu Leu Ala Gly Pro Val Gly Cys Leu Ser Arg Gln
 20 25 30
 Glu Leu Phe Pro Phe Gly Pro Gly Gln Gly Asp Leu Glu Leu Glu Asp
 35 40 45
 Gly Asp Asp Phe Val Ser Pro Ala Leu Glu Leu Ser Gly Ala Leu Arg
 50 55 60
 Phe Tyr Asp Arg Ser Asp Ile Asp Ala Val Tyr Val Thr Thr Asn Gly
 65 70 75 80
 Ile Ile Ala Thr Ser Glu Pro Pro Ala Lys Glu Ser His Pro Gly Leu
 85 90 95
 Phe Pro Pro Thr Phe Gly Ala Val Ala Pro Phe Leu Ala Asp Leu Asp
 100 105 110
 Thr Thr Asp Gly Leu Gly Lys Val Tyr Tyr Arg Glu Asp Leu Ser Pro
 115 120 125
 Ser Ile Thr Gln Arg Ala Ala Glu Cys Val His Arg Gly Phe Pro Glu
 130 135 140

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Ile	Ser	Phe	Gln	Pro	Ser	Ser	Ala	Val	Val	Val	Thr	Trp	Glu	Ser	Val	145	150	155	160
Ala	Pro	Tyr	Gln	Gly	Pro	Ser	Arg	Asp	Pro	Asp	Gln	Lys	Gly	Lys	Arg	165	170	175	
Asn	Thr	Phe	Gln	Ala	Val	Leu	Ala	Ser	Ser	Asp	Ser	Ser	Ser	Tyr	Ala	180	185	190	
Ile	Phe	Leu	Tyr	Pro	Glu	Asp	Gly	Leu	Gln	Phe	His	Thr	Thr	Phe	Ser	195	200	205	
Lys	Lys	Glu	Asn	Asn	Gln	Val	Pro	Ala	Val	Val	Ala	Phe	Ser	Gln	Gly	210	215	220	
Ser	Val	Gly	Phe	Leu	Trp	Lys	Ser	Asn	Gly	Ala	Tyr	Asn	Ile	Phe	Ala	225	230	235	240
Asn	Asp	Arg	Glu	Ser	Ile	Glu	Asn	Leu	Ala	Lys	Ser	Ser	Asn	Ser	Gly	245	250	255	
Gln	Gln	Gly	Val	Trp	Val	Phe	Glu	Ile	Gly	Ser	Pro	Ala	Thr	Thr	Asn	260	265	270	
Gly	Val	Val	Pro	Ala	Asp	Val	Ile	Leu	Gly	Thr	Glu	Asp	Gly	Ala	Glu	275	280	285	
Tyr	Asp	Asp	Glu	Asp	Glu	Asp	Tyr	Asp	Leu	Ala	Thr	Thr	Arg	Leu	Gly	290	295	300	
Leu	Glu	Asp	Val	Gly	Thr	Thr	Pro	Phe	Ser	Tyr	Lys	Ala	Leu	Arg	Arg	305	310	315	320
Gly	Gly	Ala	Asp	Thr	Tyr	Ser	Val	Pro	Ser	Val	Leu	Ser	Pro	Arg	Arg	325	330	335	
Ala	Ala	Thr	Glu	Arg	Pro	Leu	Gly	Pro	Pro	Thr	Glu	Arg	Thr	Arg	Ser	340	345	350	
Phe	Gln	Leu	Ala	Val	Glu	Thr	Phe	His	Gln	Gln	His	Pro	Gln	Val	Ile	355	360	365	
Asp	Val	Asp	Glu	Val	Glu	Glu	Thr	Gly	Val	Val	Phe	Ser	Tyr	Asn	Thr	370	375	380	
Asp	Ser	Arg	Gln	Thr	Cys	Ala	Asn	Asn	Arg	His	Gln	Cys	Ser	Val	His	385	390	395	400
Ala	Glu	Cys	Arg	Asp	Tyr	Ala	Thr	Gly	Phe	Cys	Cys	Ser	Cys	Val	Ala	405	410	415	
Gly	Tyr	Thr	Gly	Asn	Gly	Arg	Gln	Cys	Val	Ala	Glu	Gly	Ser	Pro	Gln	420	425	430	
Arg	Val	Asn	Gly	Lys	Val	Lys	Gly	Arg	Ile	Phe	Val	Gly	Ser	Ser	Gln	435	440	445	
Val	Pro	Ile	Val	Phe	Glu	Asn	Thr	Asp	Leu	His	Ser	Tyr	Val	Val	Met	450	455	460	

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Asn	His	Gly	Arg	Ser	Tyr	Thr	Ala	Ile	Ser	Thr	Ile	Pro	Glu	Thr	Val	465	470	475	480
Gly	Tyr	Ser	Leu	Leu	Pro	Leu	Ala	Pro	Val	Gly	Gly	Ile	Ile	Gly	Trp	485	490	495	
Met	Phe	Ala	Val	Glu	Gln	Asp	Gly	Phe	Lys	Asn	Gly	Phe	Ser	Ile	Thr	500	505	510	
Gly	Gly	Glu	Phe	Thr	Arg	Gln	Ala	Glu	Val	Thr	Phe	Val	Gly	His	Pro	515	520	525	
Gly	Asn	Leu	Val	Ile	Lys	Gln	Arg	Phe	Ser	Gly	Ile	Asp	Glu	His	Gly	530	535	540	
His	Leu	Thr	Ile	Asp	Thr	Glu	Leu	Glu	Gly	Arg	Val	Pro	Gln	Ile	Pro	545	550	555	560
Phe	Gly	Ser	Ser	Val	His	Ile	Glu	Pro	Tyr	Thr	Glu	Leu	Tyr	His	Tyr	565	570	575	
Ser	Thr	Ser	Val	Ile	Thr	Ser	Ser	Ser	Thr	Arg	Glu	Tyr	Thr	Val	Thr	580	585	590	
Glu	Pro	Glu	Arg	Asp	Gly	Ala	Ser	Pro	Ser	Arg	Ile	Tyr	Thr	Tyr	Gln	595	600	605	
Trp	Arg	Gln	Thr	Ile	Thr	Phe	Gln	Glu	Cys	Val	His	Asp	Asp	Ser	Arg	610	615	620	
Pro	Ala	Leu	Pro	Ser	Thr	Gln	Gln	Leu	Ser	Val	Asp	Ser	Val	Phe	Val	625	630	635	640
Leu	Tyr	Asn	Gln	Glu	Glu	Lys	Ile	Leu	Arg	Tyr	Ala	Phe	Ser	Asn	Ser	645	650	655	
Ile	Gly	Pro	Val	Arg	Glu	Gly	Ser	Pro	Asp	Ala	Leu	Gln	Asn	Pro	Cys	660	665	670	
Tyr	Ile	Gly	Thr	His	Gly	Cys	Asp	Thr	Asn	Ala	Ala	Cys	Arg	Pro	Gly	675	680	685	
Pro	Arg	Thr	Gln	Phe	Thr	Cys	Glu	Cys	Ser	Ile	Gly	Phe	Arg	Gly	Asp	690	695	700	
Gly	Arg	Thr	Cys	Tyr	Asp	Ile	Asp	Glu	Cys	Ser	Glu	Gln	Pro	Ser	Val	705	710	715	720
Cys	Gly	Ser	His	Thr	Ile	Cys	Asn	Asn	His	Pro	Gly	Thr	Phe	Arg	Cys	725	730	735	
Glu	Cys	Val	Glu	Gly	Tyr	Gln	Phe	Ser	Asp	Glu	Gly	Thr	Cys	Val	Ala	740	745	750	
Val	Val	Asp	Gln	Arg	Pro	Ile	Asn	Tyr	Cys	Glu	Thr	Gly	Leu	His	Asn	755	760	765	
Cys	Asp	Ile	Pro	Gln	Arg	Ala	Gln	Cys	Ile	Tyr	Thr	Gly	Gly	Ser	Ser	770	775	780	

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Tyr Thr Cys Ser Cys Leu Pro Gly Phe Ser Gly Asp Gly Gln Ala Cys
 785 790 795 800
 Gln Asp Val Asp Glu Cys Gln Pro Ser Arg Cys His Pro Asp Ala Phe
 805 810 815
 Cys Tyr Asn Thr Pro Gly Ser Phe Thr Cys Gln Cys Lys Pro Gly Tyr
 820 825 830
 Gln Gly Asp Gly Phe Arg Cys Val Pro Gly Glu Val Glu Lys Thr Arg
 835 840 845
 Cys Gln His Glu Arg Glu His Ile Leu Gly Ala Ala Gly Ala Thr Asp
 850 855 860
 Pro Gln Arg Pro Ile Pro Pro Gly Leu Phe Val Pro Glu Cys Asp Ala
 865 870 875 880
 His Gly His Tyr Ala Pro Thr Gln Cys His Gly Ser Thr Gly Tyr Cys
 885 890 895
 Trp Cys Val Asp Arg Asp Gly Arg Glu Val Glu Gly Thr Arg Thr Arg
 900 905 910
 Pro Gly Met Thr Pro Pro Cys Leu Ser Thr Val Ala Pro Pro Ile His
 915 920 925
 Gln Gly Pro Ala Val Pro Thr Ala Val Ile Pro Leu Pro Pro Gly Thr
 930 935 940
 His Leu Leu Phe Ala Gln Thr Gly Lys Ile Glu Arg Leu Pro Leu Glu
 945 950 955 960
 Gly Asn Thr Met Arg Lys Thr Glu Ala Lys Ala Phe Leu His Val Pro
 965 970 975
 Ala Lys Val Ile Ile Gly Leu Ala Phe Asp Cys Val Asp Lys Met Val
 980 985 990
 Tyr Trp Thr Asp Ile Thr Glu Pro Ser Ile Gly Arg Ala Ser Leu His
 995 1000 1005
 Gly Gly Glu Pro Thr Thr Ile Ile Arg Gln Asp Leu Gly Ser¹ Pro
 1010 1015 1020
 Glu Gly Ile Ala Val Asp His Leu Gly Arg Asn Ile Phe Trp Thr
 1025 1030 1035
 Asp Ser Asn Leu Asp Arg Ile Glu Val Ala Lys Leu Asp Gly Thr
 1040 1045 1050
 Gln Arg Arg Val Leu Phe Glu Thr Asp Leu Val Asn Pro Arg Gly
 1055 1060 1065
 Ile Val Thr Asp Ser Val Arg Gly Asn Leu Tyr Trp Thr Asp Trp
 1070 1075 1080
 Asn Arg Asp Asn Pro Lys Ile Glu Thr Ser Tyr Met Asp Gly Thr
 1085 1090 1095

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Asn Arg Arg Ile Leu Val Gln Asp Asp Leu Gly Leu Pro Asn Gly
 1100 1105 1110
 Leu His Phe Asp Ala Phe Ser Ser Gln Leu Cys Trp Val Asp Ala
 1115 1120 1125
 Gly Thr Asn Arg Ala Glu Cys Leu Asn Pro Ser Gln Pro Ser Arg
 1130 1135 1140
 Arg Lys Ala Leu Glu Gly Leu Gln Tyr Pro Phe Ala Val Thr Ser
 1145 1150 1155
 Tyr Gly Lys Asn Leu Tyr Phe Thr Asp Trp Lys Met Asn Ser Val
 1160 1165 1170
 Val Ala Leu Asp Leu Ala Ile Ser Lys Glu Thr Asp Ala Phe Gln
 1175 1180 1185
 Pro His Lys Gln Thr Arg Leu Tyr Gly Ile Thr Thr Ala Leu Ser
 1190 1195 1200
 Gln Cys Pro Gln Gly His Asn Tyr Cys Ser Val Asn Asn Gly Gly
 1205 1210 1215
 Cys Thr His Leu Cys Leu Ala Thr Pro Gly Ser Arg Thr Cys Arg
 1220 1225 1230
 Cys Pro Asp Asn Thr Leu Gly Val Asp Cys Ile Glu Arg
 1235 1240 1245

<210> 86
 <211> 423
 <212> PRT
 <213> Homo sapiens

<400> 86

Met Ala Met Val Val Ser Ser Trp Arg Asp Pro Gln Asp Asp Val Ala
 1 5 10 15
 Gly Gly Asn Pro Gly Gly Pro Asn Pro Ala Ala Gln Ala Ala Arg Gly
 20 25 30
 Gly Gly Gly Gly Ala Gly Glu Gln Gln Gln Gln Ala Gly Ser Gly Ala
 35 40 45
 Pro His Thr Pro Gln Thr Pro Gly Gln Pro Gly Ala Pro Ala Thr Pro
 50 55 60
 Gly Thr Ala Gly Asp Lys Gly Gln Gly Pro Pro Gly Ser Gly Gln Ser
 65 70 75 80
 Gln Gln His Ile Glu Cys Val Val Cys Gly Asp Lys Ser Ser Gly Lys
 85 90 95
 His Tyr Gly Gln Phe Thr Cys Glu Gly Cys Lys Ser Phe Phe Lys Arg
 100 105 110
 Ser Val Arg Arg Asn Leu Thr Tyr Thr Cys Arg Ala Asn Arg Asn Cys

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115	120	125
Pro Ile Asp Gln His His Arg Asn Gln Cys Gln Tyr Cys Arg Leu Lys		
130	135	140
Lys Cys Leu Lys Val Gly Met Arg Arg Glu Ala Val Gln Arg Gly Arg		
145	150	155
Met Pro Pro Thr Gln Pro Asn Pro Gly Gln Tyr Ala Leu Thr Asn Gly		
	165	170
Asp Pro Leu Asn Gly His Cys Tyr Leu Ser Gly Tyr Ile Ser Leu Leu		
	180	185
Leu Arg Ala Glu Pro Tyr Pro Thr Ser Arg Tyr Gly Ser Gln Cys Met		
	195	200
Gln Pro Asn Asn Ile Met Gly Ile Glu Asn Ile Cys Glu Leu Ala Ala		
	210	215
Arg Leu Leu Phe Ser Ala Val Glu Trp Ala Arg Asn Ile Pro Phe Phe		
	225	230
Pro Asp Leu Gln Ile Thr Asp Gln Val Ser Leu Leu Arg Leu Thr Trp		
	245	250
Ser Glu Leu Phe Val Leu Asn Ala Ala Gln Cys Ser Met Pro Leu His		
	260	265
Val Ala Pro Leu Leu Ala Ala Ala Gly Leu His Ala Ser Pro Met Ser		
	275	280
Ala Asp Arg Val Val Ala Phe Met Asp His Ile Arg Ile Phe Gln Glu		
	290	295
Gln Val Glu Lys Leu Lys Ala Leu His Val Asp Ser Ala Glu Tyr Ser		
	305	310
Cys Leu Lys Ala Ile Val Leu Phe Thr Ser Asp Ala Cys Gly Leu Ser		
	325	330
Asp Ala Ala His Ile Glu Ser Leu Gln Glu Lys Ser Gln Cys Ala Leu		
	340	345
Glu Glu Tyr Val Arg Ser Gln Tyr Pro Asn Gln Pro Ser Arg Phe Gly		
	355	360
Lys Leu Leu Leu Arg Leu Pro Ser Leu Arg Thr Val Ser Ser Ser Val		
	370	375
Ile Glu Gln Leu Phe Phe Val Arg Leu Val Gly Lys Thr Pro Ile Glu		
	385	390
Thr Leu Ile Arg Asp Met Leu Leu Ser Gly Ser Ser Phe Asn Trp Pro		
	405	410
Tyr Met Ser Ile Gln Cys Ser		
	420	

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<211> 534

<212> PRT

<213> Homo sapiens

<400> 87

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Met Ile Trp Tyr Ile Leu Ile Ile Gly Ile Leu Leu Pro Gln Ser Leu
1           5           10           15

Ala His Pro Gly Phe Phe Thr Ser Ile Gly Gln Met Thr Asp Leu Ile
          20           25           30

His Thr Glu Lys Asp Leu Val Thr Ser Leu Lys Asp Tyr Ile Lys Ala
      35           40           45

Glu Glu Asp Lys Leu Glu Gln Ile Lys Lys Trp Ala Glu Lys Leu Asp
      50           55           60

Arg Leu Thr Ser Thr Ala Thr Lys Asp Pro Glu Gly Phe Val Gly His
65           70           75           80

Pro Val Asn Ala Phe Lys Leu Met Lys Arg Leu Asn Thr Glu Trp Ser
          85           90           95

Glu Leu Glu Asn Leu Val Leu Lys Asp Met Ser Asp Gly Phe Ile Ser
          100          105          110

Asn Leu Thr Ile Gln Arg Pro Val Leu Ser Asn Asp Glu Asp Gln Val
      115           120           125

Gly Ala Ala Lys Ala Leu Leu Arg Leu Gln Asp Thr Tyr Asn Leu Asp
      130           135           140

Thr Asp Thr Ile Ser Lys Gly Asn Leu Pro Gly Val Lys His Lys Ser
145           150           155           160

Phe Leu Thr Ala Glu Asp Cys Phe Glu Leu Gly Lys Val Ala Tyr Thr
          165           170           175

Glu Ala Asp Tyr Tyr His Thr Glu Leu Trp Met Glu Gln Ala Leu Arg
          180           185           190

Gln Leu Asp Glu Gly Glu Ile Ser Thr Ile Asp Lys Val Ser Val Leu
      195           200           205

Asp Tyr Leu Ser Tyr Ala Val Tyr Gln Gln Gly Asp Leu Asp Lys Ala
      210           215           220

Leu Leu Leu Thr Lys Lys Leu Leu Glu Leu Asp Pro Glu His Gln Arg
225           230           235           240

Ala Asn Gly Asn Leu Lys Tyr Phe Glu Tyr Ile Met Ala Lys Glu Lys
          245           250           255

Asp Val Asn Lys Ser Ala Ser Asp Asp Gln Ser Asp Gln Lys Thr Thr
          260           265           270

Pro Lys Lys Lys Gly Val Ala Val Asp Tyr Leu Pro Glu Arg Gln Lys
      275           280           285

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Tyr Glu Met Leu Cys Arg Gly Glu Gly Ile Lys Met Thr Pro Arg Arg
 290 295 300
 Gln Lys Lys Leu Phe Cys Arg Tyr His Asp Gly Asn Arg Asn Pro Lys
 305 310 315 320
 Phe Ile Leu Ala Pro Ala Lys Gln Glu Asp Glu Trp Asp Lys Pro Arg
 325 330 335
 Ile Ile Arg Phe His Asp Ile Ile Ser Asp Ala Glu Ile Glu Ile Val
 340 345 350
 Lys Asp Leu Ala Lys Pro Arg Leu Ser Arg Ala Thr Val His Asp Pro
 355 360 365
 Glu Thr Gly Lys Leu Thr Thr Ala Gln Tyr Arg Val Ser Lys Ser Ala
 370 375 380
 Trp Leu Ser Gly Tyr Glu Asn Pro Val Val Ser Arg Ile Asn Met Arg
 385 390 395 400
 Ile Gln Asp Leu Thr Gly Leu Asp Val Ser Thr Ala Glu Glu Leu Gln
 405 410 415
 Val Ala Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro His Phe Asp Phe
 420 425 430
 Ala Arg Lys Asp Glu Pro Asp Ala Phe Lys Glu Leu Gly Thr Gly Asn
 435 440 445
 Arg Ile Ala Thr Trp Leu Phe Tyr Met Ser Asp Val Ser Ala Gly Gly
 450 455 460
 Ala Thr Val Phe Pro Glu Val Gly Ala Ser Val Trp Pro Lys Lys Gly
 465 470 475 480
 Thr Ala Val Phe Trp Tyr Asn Leu Phe Ala Ser Gly Glu Gly Asp Tyr
 485 490 495
 Ser Thr Arg His Ala Ala Cys Pro Val Leu Val Gly Asn Lys Trp Val
 500 505 510
 Ser Asn Lys Trp Leu His Glu Arg Gly Gln Glu Phe Arg Arg Pro Cys
 515 520 525
 Thr Leu Ser Glu Leu Glu
 530
 <210> 88
 <211> 162
 <212> PRT
 <213> Homo sapiens
 <400> 88
 Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys Leu Ala
 1 5 10 15
 Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser Leu Met
 20 25 30

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Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro
 35 40 45

Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn
 50 55 60

Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Gly Asn Pro Lys
 65 70 75 80

Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp
 85 90 95

Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr
 100 105 110

Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu
 115 120 125

Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro
 130 135 140

Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys
 145 150 155 160

Arg Phe

<210> 89
 <211> 449
 <212> PRT
 <213> Homo sapiens

<400> 89

Met Leu Pro Ala Ala Thr Ala Ser Leu Leu Gly Pro Leu Leu Thr Ala
 1 5 10 15

Cys Ala Leu Leu Pro Phe Ala Gln Gly Gln Thr Pro Asn Tyr Thr Arg
 20 25 30

Pro Val Phe Leu Cys Gly Gly Asp Val Lys Gly Glu Ser Gly Tyr Val
 35 40 45

Ala Ser Glu Gly Phe Pro Asn Ser Tyr Pro Pro Asn Lys Glu Cys Ile
 50 55 60

Trp Thr Ile Thr Val Pro Glu Gly Gln Thr Val Ser Leu Ser Phe Arg
 65 70 75 80

Val Phe Asp Leu Glu Leu His Pro Ala Cys Arg Tyr Asp Ala Leu Glu
 85 90 95

Val Phe Ala Gly Ser Gly Thr Ser Gly Gln Arg Leu Gly Arg Phe Cys
 100 105 110

Gly Thr Phe Arg Pro Ala Pro Leu Val Ala Pro Gly Asn Gln Val Thr
 115 120 125

Leu Arg Met Thr Thr Asp Glu Gly Thr Gly Gly Arg Gly Phe Leu Leu

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130	135	140
Trp Tyr Ser Gly Arg Ala Thr Ser Gly Ser Glu His Gln Phe Cys Gly		
145	150	155 160
Gly Arg Leu Glu Lys Ala Gln Gly Thr Leu Thr Thr Pro Asn Trp Pro		
	165	170 175
Glu Ser Asp Tyr Pro Pro Gly Ile Ser Cys Ser Trp His Ile Ile Ala		
	180	185 190
Pro Pro Asp Gln Val Ile Ala Leu Thr Phe Glu Lys Phe Asp Leu Glu		
	195	200 205
Pro Asp Thr Tyr Cys Arg Tyr Asp Ser Val Ser Val Phe Asn Gly Ala		
	210	215 220
Val Ser Asp Asp Ser Arg Arg Leu Gly Lys Phe Cys Gly Asp Ala Val		
	225	230 235 240
Pro Gly Ser Ile Ser Ser Glu Gly Asn Glu Leu Leu Val Gln Phe Val		
	245	250 255
Ser Asp Leu Ser Val Thr Ala Asp Gly Phe Ser Ala Ser Tyr Lys Thr		
	260	265 270
Leu Pro Arg Gly Thr Ala Lys Glu Gly Gln Gly Pro Gly Pro Lys Arg		
	275	280 285
Gly Thr Glu Pro Lys Val Lys Leu Pro Pro Lys Ser Gln Pro Pro Glu		
	290	295 300
Lys Thr Glu Glu Ser Pro Ser Ala Pro Asp Ala Pro Thr Cys Pro Lys		
	305	310 315 320
Gln Cys Arg Arg Thr Gly Thr Leu Gln Ser Asn Phe Cys Ala Ser Ser		
	325	330 335
Leu Val Val Thr Ala Thr Val Lys Ser Met Val Arg Glu Pro Gly Glu		
	340	345 350
Gly Leu Ala Val Thr Val Ser Leu Ile Gly Ala Tyr Lys Thr Gly Gly		
	355	360 365
Leu Asp Leu Pro Thr Pro Pro Thr Gly Ala Ser Leu Lys Phe Tyr Val		
	370	375 380
Pro Cys Lys Gln Cys Pro Pro Met Lys Lys Gly Val Ser Tyr Leu Leu		
	385	390 395 400
Met Gly Gln Val Glu Glu Asn Arg Gly Pro Val Leu Pro Pro Glu Ser		
	405	410 415
Phe Val Val Leu His Arg Pro Asn Gln Asp Gln Ile Leu Thr Asn Leu		
	420	425 430
Ser Lys Arg Lys Cys Pro Ser Gln Pro Val Arg Ala Ala Ala Ser Gln		
	435	440 445

Asp

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<210> 90
 <211> 1089
 <212> PRT
 <213> Homo sapiens

<400> 90

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Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
1              5              10              15

Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
              20              25              30

Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
              35              40              45

Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
              50              55              60

Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65              70              75              80

Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
              85              90              95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
              100              105              110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
              115              120              125

Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
              130              135              140

Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145              150              155              160

Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
              165              170              175

Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
              180              185              190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
              195              200              205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
210              215              220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225              230              235              240

Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
              245              250              255

Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
              260              265              270

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Tyr	Thr	Leu	Thr	Val	Pro	Glu	Ala	Thr	Val	Lys	Asp	Ser	Gly	Asp	Tyr	275	280	285
Glu	Cys	Ala	Ala	Arg	Gln	Ala	Thr	Arg	Glu	Val	Lys	Glu	Met	Lys	Lys	290	295	300
Val	Thr	Ile	Ser	Val	His	Glu	Lys	Gly	Phe	Ile	Glu	Ile	Lys	Pro	Thr	305	310	315
Phe	Ser	Gln	Leu	Glu	Ala	Val	Asn	Leu	His	Glu	Val	Lys	His	Phe	Val	325	330	335
Val	Glu	Val	Arg	Ala	Tyr	Pro	Pro	Pro	Arg	Ile	Ser	Trp	Leu	Lys	Asn	340	345	350
Asn	Leu	Thr	Leu	Ile	Glu	Asn	Leu	Thr	Glu	Ile	Thr	Thr	Asp	Val	Glu	355	360	365
Lys	Ile	Gln	Glu	Ile	Arg	Tyr	Arg	Ser	Lys	Leu	Lys	Leu	Ile	Arg	Ala	370	375	380
Lys	Glu	Glu	Asp	Ser	Gly	His	Tyr	Thr	Ile	Val	Ala	Gln	Asn	Glu	Asp	385	390	395
Ala	Val	Lys	Ser	Tyr	Thr	Phe	Glu	Leu	Leu	Thr	Gln	Val	Pro	Ser	Ser	405	410	415
Ile	Leu	Asp	Leu	Val	Asp	Asp	His	His	Gly	Ser	Thr	Gly	Gly	Gln	Thr	420	425	430
Val	Arg	Cys	Thr	Ala	Glu	Gly	Thr	Pro	Leu	Pro	Asp	Ile	Glu	Trp	Met	435	440	445
Ile	Cys	Lys	Asp	Ile	Lys	Lys	Cys	Asn	Asn	Glu	Thr	Ser	Trp	Thr	Ile	450	455	460
Leu	Ala	Asn	Asn	Val	Ser	Asn	Ile	Ile	Thr	Glu	Ile	His	Ser	Arg	Asp	465	470	475
Arg	Ser	Thr	Val	Glu	Gly	Arg	Val	Thr	Phe	Ala	Lys	Val	Glu	Glu	Thr	485	490	495
Ile	Ala	Val	Arg	Cys	Leu	Ala	Lys	Asn	Leu	Leu	Gly	Ala	Glu	Asp	Arg	500	505	510
Glu	Leu	Lys	Leu	Val	Ala	Pro	Thr	Leu	Arg	Ser	Glu	Leu	Thr	Val	Ala	515	520	525
Ala	Ala	Val	Leu	Val	Leu	Leu	Val	Ile	Val	Ile	Ile	Ser	Leu	Ile	Val	530	535	540
Leu	Val	Val	Ile	Trp	Lys	Gln	Lys	Pro	Arg	Tyr	Glu	Ile	Arg	Trp	Arg	545	550	555
Val	Ile	Glu	Ser	Ile	Ser	Pro	Asp	Gly	His	Glu	Tyr	Ile	Tyr	Val	Asp	565	570	575
Pro	Met	Gln	Leu	Pro	Tyr	Asp	Ser	Arg	Trp	Glu	Phe	Pro	Arg	Asp	Gly	580	585	590

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Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val
 595 600 605
 Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
 610 615 620
 Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
 625 630 635 640
 Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
 645 650 655
 Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
 660 665 670
 Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys
 675 680 685
 Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
 690 695 700
 Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
 705 710 715 720
 Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
 725 730 735
 Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
 740 745 750
 Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
 755 760 765
 Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
 770 775 780
 Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
 785 790 795 800
 Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
 805 810 815
 Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
 820 825 830
 Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
 835 840 845
 Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
 850 855 860
 Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
 865 870 875 880
 Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
 885 890 895
 Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
 900 905 910

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Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
 915 920 925
 Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
 930 935 940
 His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
 945 950 955 960
 Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
 965 970 975
 Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
 980 985 990
 Tyr Lys Asn Glu Glu Asp Lys Leu Lys Asp Trp Glu Gly Gly Leu Asp
 995 1000 1005
 Glu Gln Arg Leu Ser Ala Asp Ser Gly Tyr Ile Ile Pro Leu Pro
 1010 1015 1020
 Asp Ile Asp Pro Val Pro Glu Glu Glu Asp Leu Gly Lys Arg Asn
 1025 1030 1035
 Arg His Ser Ser Gln Thr Ser Glu Glu Ser Ala Ile Glu Thr Gly
 1040 1045 1050
 Ser Ser Ser Ser Thr Phe Ile Lys Arg Glu Asp Glu Thr Ile Glu
 1055 1060 1065
 Asp Ile Asp Met Met Asp Asp Ile Gly Ile Asp Ser Ser Asp Leu
 1070 1075 1080
 Val Glu Asp Ser Phe Leu
 1085
 <210> 91
 <211> 318
 <212> PRT
 <213> Homo sapiens
 <400> 91
 Met Pro Asn Ile Lys Ile Phe Ser Gly Ser Ser His Gln Asp Leu Ser
 1 5 10 15
 Gln Lys Ile Ala Asp Arg Leu Gly Leu Glu Leu Gly Lys Val Val Thr
 20 25 30
 Lys Lys Phe Ser Asn Gln Glu Thr Cys Val Glu Ile Gly Glu Ser Val
 35 40 45
 Arg Gly Glu Asp Val Tyr Ile Val Gln Ser Gly Cys Gly Glu Ile Asn
 50 55 60
 Asp Asn Leu Met Glu Leu Leu Ile Met Ile Asn Ala Cys Lys Ile Ala
 65 70 75 80
 Ser Ala Ser Arg Val Thr Ala Val Ile Pro Cys Phe Pro Tyr Ala Arg
 85 90 95

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Gln Asp Lys Lys Asp Lys Ser Arg Ala Pro Ile Ser Ala Lys Leu Val
 100 105 110
 Ala Asn Met Leu Ser Val Ala Gly Ala Asp His Ile Ile Thr Met Asp
 115 120 125
 Leu His Ala Ser Gln Ile Gln Gly Phe Phe Asp Ile Pro Val Asp Asn
 130 135 140
 Leu Tyr Ala Glu Pro Ala Val Leu Lys Trp Ile Arg Glu Asn Ile Ser
 145 150 155 160
 Glu Trp Arg Asn Cys Thr Ile Val Ser Pro Asp Ala Gly Gly Ala Lys
 165 170 175
 Arg Val Thr Ser Ile Ala Asp Arg Leu Asn Val Asp Phe Ala Leu Ile
 180 185 190
 His Lys Glu Arg Lys Lys Ala Asn Glu Val Asp Arg Met Val Leu Val
 195 200 205
 Gly Asp Val Lys Asp Arg Val Ala Ile Leu Val Asp Asp Met Ala Asp
 210 215 220
 Thr Cys Gly Thr Ile Cys His Ala Ala Asp Lys Leu Leu Ser Ala Gly
 225 230 235 240
 Ala Thr Arg Val Tyr Ala Ile Leu Thr His Gly Ile Phe Ser Gly Pro
 245 250 255
 Ala Ile Ser Arg Ile Asn Asn Ala Cys Phe Glu Ala Val Val Val Thr
 260 265 270
 Asn Thr Ile Pro Gln Glu Asp Lys Met Lys His Cys Ser Lys Ile Gln
 275 280 285
 Val Ile Asp Ile Ser Met Ile Leu Ala Glu Ala Ile Arg Arg Thr His
 290 295 300
 Asn Gly Glu Ser Val Ser Tyr Leu Phe Ser His Val Pro Leu
 305 310 315

<210> 92

<211> 318

<212> PRT

<213> Homo sapiens

<400> 92

Met Pro Asn Ile Val Leu Phe Ser Gly Ser Ser His Gln Asp Leu Ser
 1 5 10 15
 Gln Arg Val Ala Asp Arg Leu Gly Leu Glu Leu Gly Lys Val Val Thr
 20 25 30
 Lys Lys Phe Ser Asn Gln Glu Thr Ser Val Glu Ile Gly Glu Ser Val
 35 40 45
 Arg Gly Glu Asp Val Tyr Ile Ile Gln Ser Gly Cys Gly Glu Ile Asn

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50					55					60					
Asp	Asn	Leu	Met	Glu	Leu	Leu	Ile	Met	Ile	Asn	Ala	Cys	Lys	Ile	Ala
65					70					75					80
Ser	Ser	Ser	Arg	Val	Thr	Ala	Val	Ile	Pro	Cys	Phe	Pro	Tyr	Ala	Arg
				85					90					95	
Gln	Asp	Lys	Lys	Asp	Lys	Ser	Arg	Ala	Pro	Ile	Ser	Ala	Lys	Leu	Val
			100					105					110		
Ala	Asn	Met	Leu	Ser	Val	Ala	Gly	Ala	Asp	His	Ile	Ile	Thr	Met	Asp
		115					120					125			
Leu	His	Ala	Ser	Gln	Ile	Gln	Gly	Phe	Phe	Asp	Ile	Pro	Val	Asp	Asn
	130					135					140				
Leu	Tyr	Ala	Glu	Pro	Ala	Val	Leu	Gln	Trp	Ile	Arg	Glu	Asn	Ile	Ala
145					150					155					160
Glu	Trp	Lys	Asn	Cys	Ile	Ile	Val	Ser	Pro	Asp	Ala	Gly	Gly	Ala	Lys
			165						170					175	
Arg	Val	Thr	Ser	Ile	Ala	Asp	Arg	Leu	Asn	Val	Glu	Phe	Ala	Leu	Ile
			180					185					190		
His	Lys	Glu	Arg	Lys	Lys	Ala	Asn	Glu	Val	Asp	Arg	Met	Val	Leu	Val
	195					200						205			
Gly	Asp	Val	Lys	Asp	Arg	Val	Ala	Ile	Leu	Val	Asp	Asp	Met	Ala	Asp
	210					215					220				
Thr	Cys	Gly	Thr	Ile	Cys	His	Ala	Ala	Asp	Lys	Leu	Leu	Ser	Ala	Gly
225					230					235					240
Ala	Thr	Lys	Val	Tyr	Ala	Ile	Leu	Thr	His	Gly	Ile	Phe	Ser	Gly	Pro
			245						250					255	
Ala	Ile	Ser	Arg	Ile	Asn	Asn	Ala	Ala	Phe	Glu	Ala	Val	Val	Val	Thr
			260					265					270		
Asn	Thr	Ile	Pro	Gln	Glu	Asp	Lys	Met	Lys	His	Cys	Thr	Lys	Ile	Gln
	275					280					285				
Val	Ile	Asp	Ile	Ser	Met	Ile	Leu	Ala	Glu	Ala	Ile	Arg	Arg	Thr	His
	290					295					300				
Asn	Gly	Glu	Ser	Val	Ser	Tyr	Leu	Phe	Ser	His	Val	Pro	Leu		
305					310					315					
<210> 93															
<211> 244															
<212> PRT															
<213> Homo sapiens															
<400> 93															
Met	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Gly	Glu	Ala	Arg	Arg	Val	Leu	Val
1					5					10					15

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Gly Gly Arg Gly Ala Leu Gly Ser Arg Cys Val Gln Ala Phe Arg Ala
 20 25 30
 Arg Asn Trp Trp Val Ala Ser Val Asp Val Val Glu Asn Glu Glu Ala
 35 40 45
 Ser Ala Thr Ile Ile Val Lys Met Thr Asp Ser Phe Thr Glu Gln Ala
 50 55 60
 Asp Gln Val Thr Ala Glu Val Gly Lys Leu Leu Gly Glu Glu Lys Val
 65 70 75 80
 Asp Ala Ile Leu Cys Val Ala Gly Gly Trp Ala Gly Gly Asn Ala Lys
 85 90 95
 Ser Lys Ser Leu Phe Lys Asn Cys Asp Leu Met Trp Lys Gln Ser Ile
 100 105 110
 Trp Thr Ser Thr Ile Ser Ser His Leu Ala Thr Lys His Leu Lys Glu
 115 120 125
 Gly Gly Leu Leu Thr Leu Ala Gly Ala Lys Ala Ala Leu Asp Gly Thr
 130 135 140
 Pro Gly Met Ile Gly Tyr Gly Met Ala Lys Gly Ala Val His Gln Leu
 145 150 155 160
 Cys Gln Ser Leu Ala Gly Lys Asn Ser Gly Met Pro Pro Gly Ala Ala
 165 170 175
 Ala Ile Ala Val Leu Pro Val Thr Leu Asp Thr Pro Met Asn Arg Lys
 180 185 190
 Ser Met Pro Glu Ala Asp Phe Ser Ser Trp Thr Pro Leu Glu Phe Leu
 195 200 205
 Val Glu Thr Phe His Asp Trp Ile Thr Gly Lys Asn Arg Pro Ser Ser
 210 215 220
 Gly Ser Leu Ile Gln Val Val Thr Thr Glu Gly Arg Thr Glu Leu Thr
 225 230 235 240

Pro Ala Tyr Phe

<210> 94
 <211> 331
 <212> PRT
 <213> Homo sapiens

<400> 94

Met Gly Thr Pro Gln Lys Asp Val Ile Ile Lys Ser Asp Ala Pro Asp
 1 5 10 15
 Thr Leu Leu Leu Glu Lys His Ala Asp Tyr Ile Ala Ser Tyr Gly Ser
 20 25 30
 Lys Lys Asp Asp Tyr Glu Tyr Cys Met Ser Glu Tyr Leu Arg Met Ser
 35 40 45

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Gly Ile Tyr Trp Gly Leu Thr Val Met Asp Leu Met Gly Gln Leu His
 50 55 60
 Arg Met Asn Arg Glu Glu Ile Leu Ala Phe Ile Lys Ser Cys Gln His
 65 70 75 80
 Glu Cys Gly Gly Ile Ser Ala Ser Ile Gly His Asp Pro His Leu Leu
 85 90 95
 Tyr Thr Leu Ser Ala Val Gln Ile Leu Thr Leu Tyr Asp Ser Ile Asn
 100 105 110
 Val Ile Asp Val Asn Lys Val Val Glu Tyr Val Lys Gly Leu Gln Lys
 115 120 125
 Glu Asp Gly Ser Phe Ala Gly Asp Ile Trp Gly Glu Ile Asp Thr Arg
 130 135 140
 Phe Ser Phe Cys Ala Val Ala Thr Leu Ala Leu Leu Gly Lys Leu Asp
 145 150 155 160
 Ala Ile Asn Val Glu Lys Ala Ile Glu Phe Val Leu Ser Cys Met Asn
 165 170 175
 Phe Asp Gly Gly Phe Gly Cys Arg Pro Gly Ser Glu Ser His Ala Gly
 180 185 190
 Gln Ile Tyr Cys Cys Thr Gly Phe Leu Ala Ile Thr Ser Gln Leu His
 195 200 205
 Gln Val Asn Ser Asp Leu Leu Gly Trp Trp Leu Cys Glu Arg Gln Leu
 210 215 220
 Pro Ser Gly Gly Leu Asn Gly Arg Pro Glu Lys Leu Pro Asp Val Cys
 225 230 235 240
 Tyr Ser Trp Trp Val Leu Ala Ser Leu Lys Ile Ile Gly Arg Leu His
 245 250 255
 Trp Ile Asp Arg Glu Lys Leu Arg Asn Phe Ile Leu Ala Cys Gln Asp
 260 265 270
 Glu Glu Thr Gly Gly Phe Ala Asp Arg Pro Gly Asp Met Val Asp¹ Pro
 275 280 285
 Phe His Thr Leu Phe Gly Ile Ala Gly Leu Ser Leu Leu Gly Glu Glu
 290 295 300
 Gln Ile Lys Pro Val Asn Pro Val Phe Cys Met Pro Glu Glu Val Leu
 305 310 315 320
 Gln Arg Val Asn Val Gln Pro Glu Leu Val Ser
 325 330

<210> 95

<211> 93

<212> PRT

<213> Homo sapiens

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<400> 95

Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1 5 10 15

Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
20 25 30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
35 40 45

Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
50 55 60

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65 70 75 80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
85 90

<210> 96

<211> 381

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (59)..(59)

<223> Xaa = any amino acid

<220>

<221> UNSURE

<222> (300)..(300)

<223> Xaa = any amino acid

<220>

<221> UNSURE

<222> (318)..(318)

<223> Xaa = any amino acid

<220>

<221> UNSURE

<222> (330)..(330)

<223> Xaa = any amino acid

<220>

<221> UNSURE

<222> (345)..(345)

<223> Xaa = any amino acid

<220>

<221> UNSURE

<222> (352)..(352)

<223> Xaa = any amino acid

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<220>
 <221> UNSURE
 <222> (367)..(367)
 <223> Xaa = any amino acid

<220>
 <221> UNSURE
 <222> (369)..(369)
 <223> Xaa = any amino acid

<220>
 <221> UNSURE
 <222> (376)..(376)
 <223> Xaa = any amino acid

<220>
 <221> UNSURE
 <222> (378)..(378)
 <223> Xaa = any amino acid

<400> 96

Met	Trp	Arg	Ser	Leu	Gly	Leu	Ala	Leu	Ala	Leu	Cys	Leu	Leu	Pro	Ser
1				5				10						15	
Gly	Gly	Thr	Glu	Ser	Gln	Asp	Gln	Ser	Ser	Leu	Cys	Lys	Gln	Pro	Pro
			20				25						30		
Ala	Trp	Ser	Ile	Arg	Asp	Gln	Asp	Pro	Met	Leu	Asn	Ser	Asn	Gly	Ser
		35				40						45			
Val	Thr	Val	Val	Ala	Leu	Leu	Gln	Ala	Ser	Xaa	Tyr	Leu	Cys	Ile	Ile
	50				55					60					
Glu	Ala	Ser	Lys	Leu	Glu	Asp	Leu	Arg	Val	Lys	Leu	Lys	Lys	Glu	Gly
65				70				75						80	
Tyr	Ser	Asn	Ile	Ser	Tyr	Ile	Val	Val	Asn	His	Gln	Gly	Ile	Ser	Ser
			85					90					95		
Arg	Leu	Lys	Tyr	Thr	His	Leu	Lys	Asn	Lys	Val	Ser	Glu	His	Ile	Pro
			100					105					110		
Val	Tyr	Gln	Gln	Glu	Glu	Asn	Gln	Thr	Asp	Val	Trp	Thr	Leu	Leu	Asn
	115						120					125			
Gly	Ser	Lys	Asp	Asp	Phe	Leu	Ile	Tyr	Asp	Arg	Cys	Gly	Arg	Leu	Val
	130					135					140				
Tyr	His	Leu	Gly	Leu	Pro	Phe	Ser	Phe	Leu	Thr	Phe	Pro	Tyr	Val	Glu
145				150					155						160
Glu	Ala	Ile	Lys	Ile	Ala	Tyr	Cys	Glu	Lys	Lys	Cys	Gly	Asn	Cys	Ser
			165					170					175		

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Leu Thr Thr Leu Lys Asp Glu Asp Phe Cys Lys Arg Val Ser Leu Ala
 180 185 190
 Thr Val Asp Lys Thr Val Glu Thr Pro Ser Pro His Tyr His His Glu
 195 200 205
 His His His Asn His Gly His Gln His Leu Gly Ser Ser Glu Leu Ser
 210 215 220
 Glu Asn Gln Gln Pro Gly Ala Pro Asn Ala Pro Thr His Pro Ala Pro
 225 230 235 240
 Pro Gly Leu His His His His Lys His Lys Gly Gln His Arg Gln Gly
 245 250 255
 His Pro Glu Asn Arg Asp Met Pro Ala Ser Glu Asp Leu Gln Asp Leu
 260 265 270
 Gln Lys Lys Leu Cys Arg Lys Arg Cys Ile Asn Gln Leu Leu Cys Lys
 275 280 285
 Leu Pro Thr Asp Ser Glu Leu Ala Pro Arg Ser Xaa Cys Cys His Cys
 290 295 300
 Arg His Leu Ile Phe Glu Lys Thr Gly Ser Ala Ile Thr Xaa Gln Cys
 305 310 315 320
 Lys Glu Asn Leu Pro Ser Leu Cys Ser Xaa Gln Gly Leu Arg Ala Glu
 325 330 335
 Glu Asn Ile Thr Glu Ser Cys Gln Xaa Arg Leu Pro Pro Ala Ala Xaa
 340 345 350
 Gln Ile Ser Gln Gln Leu Ile Pro Thr Glu Ala Ser Ala Ser Xaa Arg
 355 360 365
 Xaa Lys Asn Gln Ala Lys Lys Xaa Glu Xaa Pro Ser Asn
 370 375 380

<210> 97
 <211> 220
 <212> PRT
 <213> Homo sapiens

<400> 97

Met Ala Ile Leu Phe Ala Val Val Ala Arg Gly Thr Thr Ile Leu Ala
 1 5 10 15
 Lys His Ala Trp Cys Gly Gly Asn Phe Leu Glu Val Thr Glu Gln Ile
 20 25 30
 Leu Ala Lys Ile Pro Ser Glu Asn Asn Lys Leu Thr Tyr Ser His Gly
 35 40 45
 Asn Tyr Leu Phe His Tyr Ile Cys Gln Asp Arg Ile Val Tyr Leu Cys
 50 55 60
 Ile Thr Asp Asp Asp Phe Glu Arg Ser Arg Ala Phe Asn Phe Leu Asn
 65 70 75 80

Glu	Ile	Lys	Lys	Arg 85	Phe	Gln	Thr	Thr	Tyr 90	Gly	Ser	Arg	Ala	Gln 95	Thr
Ala	Leu	Pro	Tyr 100	Ala	Met	Asn	Ser	Glu	Phe 105	Ser	Ser	Val	Leu	Ala 110	Ala
Gln	Leu	Lys 115	His	His	Ser	Glu	Asn 120	Lys	Gly	Leu	Asp 125	Lys	Val	Met	Glu
Thr	Gln 130	Ala	Gln	Val	Asp	Glu 135	Leu	Lys	Gly	Ile	Met 140	Val	Arg	Asn	Ile
Asp 145	Leu	Val	Ala	Gln	Arg 150	Gly	Glu	Arg	Leu	Glu 155	Leu	Leu	Ile	Asp 160	Lys
Thr	Glu	Asn	Leu 165	Val	Asp	Ser	Ser	Val	Thr 170	Phe	Lys	Thr	Thr	Ser 175	Arg
Asn	Leu	Ala	Arg 180	Ala	Met	Cys	Met	Lys 185	Asn	Leu	Lys	Leu	Thr 190	Ile	Ile
Ile	Ile	Ile 195	Val	Ser	Ile	Val	Phe 200	Ile	Tyr	Ile	Ile	Val 205	Ser	Pro	Leu
Cys	Gly 210	Gly	Phe	Thr	Trp	Pro 215	Ser	Cys	Val	Lys	Lys 220				

<400> 98

Met 1	Glu	Glu	Thr	Ala 5	Ile	Trp	Glu	Gln	His 10	Thr	Val	Thr	Leu	His 15	Arg
Ala	Pro	Gly	Phe 20	Gly	Phe	Gly	Ile	Ala 25	Ile	Ser	Gly	Gly	Arg 30	Asp	Asn
Pro	His 35	Phe	Gln	Ser	Gly	Glu	Thr 40	Ser	Ile	Val	Ile	Ser 45	Asp	Val	Leu
Lys 50	Gly	Gly	Pro	Ala	Glu	Gly 55	Gln	Leu	Gln	Glu	Asn 60	Asp	Arg	Val	Ala
Met 65	Val	Asn	Gly	Val	Ser 70	Met	Asp	Asn	Val	Glu 75	His	Ala	Phe	Ala 80	Val
Gln	Gln	Leu	Arg 85	Lys	Ser	Gly	Lys	Asn 90	Ala	Lys	Ile	Thr	Ile 95	Arg	Arg
Lys	Lys	Lys	Val 100	Gln	Ile	Pro	Val	Ser 105	Arg	Pro	Asp	Pro	Glu 110	Pro	Val
Ser	Asp 115	Asn	Glu	Glu	Asp	Ser	Tyr 120	Asp	Glu	Glu	Ile 125	His	Asp	Pro	Arg
Ser	Gly	Arg	Ser	Gly	Val	Val	Asn	Arg	Arg	Ser	Glu	Lys	Ile	Trp	Pro

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130		135		140
Arg Asp Arg Ser Ala Ser Arg Glu Arg Ser Leu Ser Pro Arg Ser Asp				
145		150		155
Arg Arg Ser Val Ala Ser Ser Gln Pro Ala Lys Pro Thr Lys Val Thr				
	165		170	175
Leu Val Lys Ser Arg Lys Asn Glu Glu Tyr Gly Leu Arg Leu Ala Ser				
	180		185	190
His Ile Phe Val Lys Glu Ile Ser Gln Asp Ser Leu Ala Ala Arg Asp				
	195		200	205
Gly Asn Ile Gln Glu Gly Asp Val Val Leu Lys Ile Asn Gly Thr Val				
	210		215	220
Thr Glu Asn Met Ser Leu Thr Asp Ala Lys Thr Leu Ile Glu Arg Ser				
	225		230	235
Lys Gly Lys Leu Lys Met Val Val Gln Arg Asp Glu Arg Ala Thr Leu				
	245		250	255
Leu Asn Val Pro Asp Leu Ser Asp Ser Ile His Ser Ala Asn Ala Ser				
	260		265	270
Glu Arg Asp Asp Ile Ser Glu Ile Gln Ser Leu Ala Ser Asp His Ser				
	275		280	285
Gly Arg Ser His Asp Arg Pro Pro Arg Arg Ser Arg Ser Arg Ser Pro				
	290		295	300
Asp Gln Arg Ser Glu Pro Ser Asp His Ser Arg His Ser Pro Gln Gln				
	305		310	315
Pro Ser Asn Gly Ser Leu Arg Ser Arg Asp Glu Glu Arg Ile Ser Lys				
	325		330	335
Pro Gly Ala Val Ser Thr Pro Val Lys His Ala Asp Asp His Thr Pro				
	340		345	350
Lys Thr Val Glu Glu Val Thr Val Glu Arg Asn Glu Lys Gln Thr Pro				
	355		360	365
Ser Leu Pro Glu Pro Lys Pro Val Tyr Ala Gln Val Gly Asn Gln Met				
	370		375	380
Trp Ile Tyr Leu Ser Val His Leu Met Val Ser Tyr Leu Ile Gln Leu				
	385		390	395
Met Lys Met Gly Phe Leu Arg Pro Ser Met Lys Leu Val Lys Phe Arg				
	405		410	415
Lys Gly Asp Ser Val Gly Leu Arg Leu Ala Gly Gly Asn Asp Val Gly				
	420		425	430
Ile Phe Val Ala Gly Val Leu Glu Asp Ser Pro Ala Ala Lys Glu Gly				
	435		440	445
Leu Glu Glu Gly Asp Gln Ile Leu Arg Val Asn Asn Val Asp Phe Thr				

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450					455					460					
Asn	Ile	Ile	Arg	Glu	Glu	Ala	Val	Leu	Phe	Leu	Leu	Asp	Leu	Pro	Lys
465					470					475					480
Gly	Glu	Glu	Val	Thr	Ile	Leu	Ala	Gln	Lys	Lys	Lys	Asp	Val	Tyr	Arg
				485					490						495
Arg	Ile	Val	Glu	Ser	Asp	Val	Gly	Asp	Ser	Phe	Tyr	Ile	Arg	Thr	His
			500					505					510		
Phe	Glu	Tyr	Glu	Lys	Glu	Ser	Pro	Tyr	Gly	Leu	Ser	Phe	Asn	Lys	Gly
		515					520					525			
Glu	Val	Phe	Arg	Ala	Val	Asp	Thr	Leu	Tyr	Asn	Gly	Lys	Leu	Gly	Ser
	530					535					540				
Trp	Leu	Ala	Ile	Arg	Ile	Gly	Lys	Asn	His	Lys	Glu	Val	Glu	Arg	Gly
545						550					555				560
Ile	Ile	Pro	Asn	Lys	Asn	Arg	Ala	Glu	Gln	Leu	Ala	Ser	Val	Gln	Tyr
				565					570						575
Thr	Leu	Pro	Lys	Thr	Ala	Gly	Gly	Asp	Arg	Ala	Asp	Phe	Trp	Arg	Phe
			580					585					590		
Arg	Gly	Leu	Arg	Ser	Ser	Lys	Arg	Asn	Leu	Arg	Lys	Ser	Arg	Glu	Asp
		595					600					605			
Leu	Ser	Ala	Gln	Pro	Val	Gln	Thr	Lys	Phe	Pro	Ala	Tyr	Glu	Arg	Val
	610					615					620				
Val	Leu	Arg	Glu	Ala	Gly	Phe	Leu	Arg	Pro	Val	Thr	Ile	Phe	Gly	Pro
625						630					635				640
Ile	Ala	Asp	Val	Ala	Arg	Glu	Lys	Leu	Ala	Arg	Glu	Glu	Pro	Asp	Ile
				645					650						655
Tyr	Gln	Ile	Ala	Lys	Ser	Glu	Pro	Arg	Asp	Ala	Gly	Thr	Asp	Gln	Arg
			660					665					670		
Ser	Ser	Gly	Tyr	Ile	Arg	Leu	His	Thr	Ile	Lys	Gln	Ile	Ile	Asp	Gln
		675					680					685			
Asp	Lys	His	Ala	Leu	Leu	Asp	Val	Thr	Pro	Asn	Ala	Val	Asp	Arg	Leu
	690					695					700				
Asn	Tyr	Ala	Gln	Trp	Tyr	Pro	Ile	Val	Val	Phe	Leu	Asn	Pro	Asp	Ser
705						710					715				720
Lys	Gln	Gly	Val	Lys	Thr	Met	Arg	Met	Arg	Leu	Cys	Pro	Glu	Ser	Arg
				725					730					735	
Lys	Ser	Ala	Arg	Lys	Leu	Tyr	Glu	Arg	Ser	His	Lys	Leu	Ala	Lys	Asn
			740					745					750		
Asn	His	His	Leu	Phe	Thr	Thr	Thr	Ile	Asn	Leu	Asn	Ser	Met	Asn	Asp
		755					760					765			
Gly	Trp	Tyr	Gly	Ala	Leu	Lys	Glu	Ala	Val	Gln	Gln	Gln	Gln	Asn	Gln

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770					775					780					
Leu	Val	Trp	Val	Ser	Glu	Gly	Lys	Ala	Asp	Gly	Ala	Thr	Ser	Asp	Asp
785					790					795					800
Leu	Asp	Leu	His	Asp	Asp	Arg	Leu	Ser	Tyr	Leu	Ser	Ala	Pro	Gly	Ser
				805					810					815	
Glu	Tyr	Ser	Met	Tyr	Ser	Thr	Asp	Ser	Arg	His	Thr	Ser	Asp	Tyr	Glu
			820					825					830		
Asp	Thr	Asp	Thr	Glu	Gly	Gly	Ala	Tyr	Thr	Asp	Gln	Glu	Leu	Asp	Glu
		835					840					845			
Thr	Leu	Asn	Asp	Glu	Val	Gly	Thr	Pro	Pro	Glu	Ser	Ala	Ile	Thr	Arg
	850					855					860				
Ser	Ser	Glu	Pro	Val	Arg	Glu	Asp	Ser	Ser	Gly	Met	His	His	Glu	Asn
865					870					875					880
Gln	Thr	Tyr	Pro	Pro	Tyr	Ser	Pro	Gln	Ala	Gln	Pro	Gln	Pro	Ile	His
				885					890					895	
Arg	Ile	Asp	Ser	Pro	Gly	Phe	Lys	Pro	Ala	Ser	Gln	Gln	Lys	Ala	Glu
			900					905					910		
Ala	Ser	Ser	Pro	Val	Pro	Tyr	Leu	Ser	Pro	Glu	Thr	Asn	Pro	Ala	Ser
			915				920					925			
Ser	Thr	Ser	Ala	Val	Asn	His	Asn	Val	Asn	Leu	Thr	Asn	Val	Arg	Leu
	930					935					940				
Glu	Glu	Pro	Thr	Pro	Ala	Pro	Ser	Thr	Ser	Tyr	Ser	Pro	Gln	Ala	Asp
945					950					955					960
Ser	Leu	Arg	Thr	Pro	Ser	Thr	Glu	Ala	Ala	His	Ile	Met	Leu	Arg	Asp
				965					970					975	
Gln	Glu	Pro	Ser	Leu	Ser	Ser	His	Val	Asp	Pro	Thr	Lys	Val	Tyr	Arg
			980					985					990		
Lys	Asp	Pro	Tyr	Pro	Glu	Glu	Met	Met	Arg	Gln	Asn	His	Val	Leu	Lys
		995					1000					1005			
Gln	Pro	Ala	Val	Ser	His	Pro	Gly	His	Arg	Pro	Asp	Lys	Glu	Pro	
	1010					1015					1020				
Asn	Leu	Thr	Tyr	Glu	Pro	Gln	Leu	Pro	Tyr	Val	Glu	Lys	Gln	Ala	
	1025					1030					1035				
Ser	Arg	Asp	Leu	Glu	Gln	Pro	Thr	Tyr	Arg	Tyr	Glu	Ser	Ser	Ser	
	1040					1045					1050				
Tyr	Thr	Asp	Gln	Phe	Ser	Arg	Asn	Tyr	Glu	His	Arg	Leu	Arg	Tyr	
	1055					1060					1065				
Glu	Asp	Arg	Val	Pro	Met	Tyr	Glu	Glu	Gln	Trp	Ser	Tyr	Tyr	Asp	
	1070					1075					1080				
Asp	Lys	Gln	Pro	Tyr	Pro	Ser	Arg	Pro	Pro	Phe	Asp	Asn	Gln	His	

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1085		1090		1095
Ser Gln Asp Leu Asp Ser	Arg Gln His Pro Glu	Glu Ser Ser Glu		
1100	1105	1110		
Arg Gly Tyr Phe Pro Arg	Phe Glu Glu Pro Ala	Pro Leu Ser Tyr		
1115	1120	1125		
Asp Ser Arg Pro Arg Tyr	Glu Gln Ala Pro Arg	Ala Ser Ala Leu		
1130	1135	1140		
Arg His Glu Glu Gln Pro	Ala Pro Gly Tyr Asp	Thr His Gly Arg		
1145	1150	1155		
Leu Arg Pro Glu Ala Gln	Pro His Pro Ser Ala	Gly Pro Lys Pro		
1160	1165	1170		
Ala Glu Ser Lys Gln Tyr	Phe Glu Gln Tyr Ser	Arg Ser Tyr Glu		
1175	1180	1185		
Gln Val Pro Pro Gln Gly	Phe Thr Ser Arg Ala	Gly His Phe Glu		
1190	1195	1200		
Pro Leu His Gly Ala Ala	Ala Val Pro Pro Leu	Ile Pro Ser Ser		
1205	1210	1215		
Gln His Lys Pro Glu Ala	Leu Pro Ser Asn Thr	Lys Pro Leu Pro		
1220	1225	1230		
Pro Pro Pro Thr Gln Thr	Glu Glu Glu Asp	Pro Ala Met Lys		
1235	1240	1245		
Pro Gln Ser Val Leu Thr	Arg Val Lys Met Phe	Glu Asn Lys Arg		
1250	1255	1260		
Ser Ala Ser Leu Glu Thr	Lys Lys Asp Val Asn	Asp Thr Gly Ser		
1265	1270	1275		
Phe Lys Pro Pro Glu Val	Ala Ser Lys Pro Ser	Gly Ala Pro Ile		
1280	1285	1290		
Ile Gly Pro Lys Pro Thr	Ser Gln Asn Gln Phe	Ser Glu His Asp		
1295	1300	1305		
Lys Thr Leu Tyr Arg Ile	Pro Glu Pro Gln Lys	Pro Gln Leu Lys		
1310	1315	1320		
Pro Pro Glu Asp Ile Val	Arg Ser Asn His Tyr	Asp Pro Glu Glu		
1325	1330	1335		
Asp Glu Glu Tyr Tyr Arg	Lys Gln Leu Ser Tyr	Phe Asp Arg Arg		
1340	1345	1350		
Ser Phe Glu Asn Lys Pro	Pro Ala His Ile Ala	Ala Ser His Leu		
1355	1360	1365		
Ser Glu Pro Ala Lys Pro	Ala His Ser Gln Asn	Gln Ser Asn Phe		
1370	1375	1380		
Ser Ser Tyr Ser Ser Lys	Gly Lys Pro Pro Glu	Ala Asp Gly Val		

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1385		1390		1395
Asp Arg Ser Phe Gly Glu Lys Arg Tyr Glu Pro Ile Gln Ala Thr				
1400		1405		1410
Pro Pro Pro Pro Pro Leu Pro Ser Gln Tyr Ala Gln Pro Ser Gln				
1415		1420		1425
Pro Val Thr Ser Ala Ser Leu His Ile His Ser Lys Gly Ala His				
1430		1435		1440
Gly Glu Gly Asn Ser Val Ser Leu Asp Phe Gln Asn Ser Leu Val				
1445		1450		1455
Ser Lys Pro Asp Pro Pro Pro Ser Gln Asn Lys Pro Ala Thr Phe				
1460		1465		1470
Arg Pro Pro Asn Arg Glu Asp Thr Ala Gln Ala Ala Phe Tyr Pro				
1475		1480		1485
Gln Lys Ser Phe Pro Asp Lys Ala Pro Val Asn Gly Thr Glu Gln				
1490		1495		1500
Thr Gln Lys Thr Val Thr Pro Ala Tyr Asn Arg Phe Thr Pro Lys				
1505		1510		1515
Pro Tyr Thr Ser Ser Ala Arg Pro Phe Glu Arg Lys Phe Glu Ser				
1520		1525		1530
Pro Lys Phe Asn His Asn Leu Leu Pro Ser Glu Thr Ala His Lys				
1535		1540		1545
Pro Asp Leu Ser Ser Lys Thr Pro Thr Ser Pro Lys Thr Leu Val				
1550		1555		1560
Lys Ser His Ser Leu Ala Gln Pro Pro Glu Phe Asp Ser Gly Val				
1565		1570		1575
Glu Thr Phe Ser Ile His Ala Glu Lys Pro Lys Tyr Gln Ile Asn				
1580		1585		1590
Asn Ile Ser Thr Val Pro Lys Ala Ile Pro Val Ser Pro Ser Ala				
1595		1600		1605
Val Glu Glu Asp Glu Asp Glu Asp Gly His Thr Val Val Ala Thr				
1610		1615		1620
Ala Arg Gly Ile Phe Asn Ser Asn Gly Gly Val Leu Ser Ser Ile				
1625		1630		1635
Glu Thr Gly Val Ser Ile Ile Ile Pro Gln Gly Ala Ile Pro Glu				
1640		1645		1650
Gly Val Glu Gln Glu Ile Tyr Phe Lys Val Cys Arg Asp Asn Ser				
1655		1660		1665
Ile Leu Pro Pro Leu Asp Lys Glu Lys Gly Glu Thr Leu Leu Ser				
1670		1675		1680
Pro Leu Val Met Cys Gly Pro His Gly Leu Lys Phe Leu Lys Pro				

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1685 1690 1695
 Val Glu Leu Arg Leu Pro His Cys Asp Pro Lys Thr Trp Gln Asn
 1700 1705 1710
 Lys Cys Leu Pro Gly Asp Pro Asn Tyr Leu Val Gly Ala Asn Cys
 1715 1720 1725
 Val Ser Val Leu Ile Asp His Phe
 1730 1735

 <210> 99
 <211> 93
 <212> PRT
 <213> Homo sapiens

 <400> 99

 Met Gln Arg Arg Gly Gln Pro Leu Glu Asn His Val Ala Leu Ile His
 1 5 10 15
 Trp Gln Ser Ala Gly Ile Pro Ala Ser Lys Val His Asn Tyr Cys Asn
 20 25 30
 Met Lys Lys Ser Arg Leu Gly Arg Ser Arg Ala Val Arg Ile Ser Gln
 35 40 45
 Pro Leu Leu Ser Pro Arg Arg Cys Pro Leu His Leu Thr Glu Arg Gly
 50 55 60
 Ala Gly Leu Leu Gln Pro Gln Pro Gln Gly Pro Val Arg Thr Pro Gly
 65 70 75 80
 Pro Pro Pro Gly Val Thr Gln Arg Pro Arg Thr Thr Glu
 85 90

 <210> 100
 <211> 582
 <212> PRT
 <213> Homo sapiens

 <400> 100

 Asp Val Ser Arg Cys Ala His Arg Ala Arg Pro Gly Ala Ile Met¹ Leu
 1 5 10 15
 Leu Leu Pro Ser Ala Ala Asp Gly Arg Gly Thr Ala Ile Thr His Ala
 20 25 30
 Leu Thr Ser Ala Ser Thr Leu Cys Gln Val Glu Pro Val Gly Arg Trp
 35 40 45
 Phe Glu Ala Phe Val Lys Arg Arg Asn Arg Asn Ala Ser Ala Ser Phe
 50 55 60
 Gln Glu Leu Glu Asp Lys Lys Glu Leu Ser Glu Glu Ser Glu Asp Glu
 65 70 75 80
 Glu Leu Gln Leu Glu Glu Phe Pro Met Leu Lys Thr Leu Asp Pro Lys
 85 90 95

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Asp	Trp	Lys	Asn	Gln	Asp	His	Tyr	Ala	Val	Leu	Gly	Leu	Gly	His	Val	
			100					105						110		
Arg	Tyr	Lys	Ala	Thr	Gln	Arg	Gln	Ile	Lys	Ala	Ala	His	Lys	Ala	Met	
		115					120					125				
Val	Leu	Lys	His	His	Pro	Asp	Lys	Arg	Lys	Ala	Ala	Gly	Glu	Pro	Ile	
	130					135						140				
Lys	Glu	Gly	Asp	Asn	Asp	Tyr	Phe	Thr	Cys	Ile	Thr	Lys	Ala	Tyr	Glu	
145					150					155					160	
Met	Leu	Ser	Asp	Pro	Val	Lys	Arg	Arg	Ala	Phe	Asn	Ser	Val	Asp	Pro	
				165					170					175		
Thr	Phe	Asp	Asn	Ser	Val	Pro	Ser	Lys	Ser	Glu	Ala	Lys	Asp	Asn	Phe	
			180					185					190			
Phe	Glu	Val	Phe	Thr	Pro	Val	Phe	Glu	Arg	Asn	Ser	Arg	Trp	Ser	Asn	
		195					200					205				
Lys	Lys	Asn	Val	Pro	Lys	Leu	Gly	Asp	Met	Asn	Ser	Ser	Phe	Glu	Asp	
	210					215					220					
Val	Asp	Ile	Phe	Tyr	Ser	Phe	Trp	Tyr	Asn	Phe	Asp	Ser	Trp	Arg	Glu	
225					230					235					240	
Phe	Ser	Tyr	Leu	Asp	Glu	Glu	Glu	Lys	Glu	Lys	Ala	Glu	Cys	Arg	Asp	
				245					250					255		
Glu	Arg	Arg	Trp	Ile	Glu	Lys	Gln	Asn	Gly	Ala	Thr	Arg	Ala	Gln	Arg	
			260					265						270		
Lys	Lys	Glu	Glu	Met	Asn	Arg	Ile	Arg	Thr	Leu	Val	Asp	Asn	Ala	Tyr	
		275					280					285				
Ser	Cys	Asp	Pro	Arg	Ile	Lys	Lys	Phe	Lys	Glu	Glu	Glu	Lys	Ala	Lys	
	290					295					300					
Lys	Glu	Ala	Glu	Lys	Lys	Ala	Lys	Ala	Glu	Ala	Lys	Arg	Lys	Glu	Gln	
305					310					315					320	
Glu	Ala	Lys	Glu	Lys	Gln	Arg	Gln	Ala	Glu	Leu	Glu	Ala	Ala	Arg	Leu	
				325					330					335		
Ala	Lys	Glu	Lys	Glu	Glu	Glu	Glu	Val	Arg	Gln	Gln	Ala	Leu	Leu	Ala	
			340					345					350			
Lys	Lys	Glu	Lys	Asp	Ile	Gln	Lys	Lys	Ala	Ile	Lys	Lys	Glu	Arg	Gln	
		355					360					365				
Lys	Leu	Arg	Asn	Ser	Cys	Lys	Ile	Glu	Glu	Ile	Asn	Glu	Gln	Ile	Arg	
	370					375					380					
Lys	Glu	Lys	Glu	Glu	Ala	Glu	Ala	Arg	Met	Arg	Gln	Ala	Ser	Lys	Asn	
385					390					395					400	
Thr	Glu	Lys	Ser	Thr	Gly	Gly	Gly	Gly	Asn	Gly	Ser	Lys	Asn	Trp	Ser	
				405					410					415		

